PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12N 15/11, 9/00, 5/10		(11) Internati nal Publication Number: WO 97/15662		
		(43) International Publication Date: 1 May 1997 (01.05.97)		
(21) International Application Number: PCT/USS (22) International Filing Date: 25 October 1996 (2)		BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,		
(30) Priority Data: 60/005,974 26 October 1995 (26.10.95) 08/584,040 11 January 1996 (11.01.96)	t t			
 (71) Applicants: RIBOZYME PHARMACEUTICALL [US/US]; 2950 Wilderness Place, Boulder, CO 803 CHIRON CORPORATION [US/US]; 4560 Horton Emeryville, CA 94608 (US). (72) Inventors: PAVCO, Pamela; 705 Barberry Circle, I CO 80026 (US). McSWIGGEN, James; 4866 Drive, Boulder, co 80301 (US). STINCHCOMB, E Old Post Road, Boulder, CO 80301 (US). ESC Jaime; 1470 Livorna Road, Alamo, CA 94507 (US). (74) Agents: HELLENKAMP, Amy, S. et al.; Lyon & Lyon Suite 4700, 633 West Fifth Street, Los Angeles, C. 	Lafayet Franki Dan; 72: COBED S).), , , , , , , , , , , , , , , , , , ,		
2066 (US). (54) Title: METHOD AND REAGENT FOR THE TRIVASCULAR ENDOTHELIAL GROWTH FA	EATMI	NT OF DISEASES OR CONDITIONS RELATED TO LEVELS OF RECEPTOR		

(57) Abstract

Nucleic acid molecule which modulates the synthesis, expression and/or stability of an mRNA encoding one or more receptors of vascular endothelial growth factor.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgystan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic	SD	Sudan
CF	Central African Republic		of Korea	SE	Sweden
CG	•	KR	Republic of Korea	SG	Singapore
	Congo Switzerland	KZ	Kazakhstan	SI	Slovenia
CH CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
	Cameroon	LK	Sri Lanka	SN	Senegal
CM		LR	Liberia	SZ	Swaziland
CN	China	LT	Lithuania	TD	Chad
CS	Czechoslovakia	LU	Luxembourg	TG	Togo
CZ	Czech Republic	LV	Latvia	TJ	Tajikistan
DE	Germany	MC	Monaco	11	Trinidad and Tobago
DK	Denmark			UA	Ukraine
EE	Estonia	MD	Republic of Moldova	บด	Uganda
ES	Spain	MG	Madagascar	US	United States of America
Fl	Finland	ML	Mali		Uzbekistan
FR	France	MN	Mongolia	UZ	Viet Nam
GA	Gabon	MR	Mauritania	VN	A ICI MAIN

1

DESCRIPTION

Method and Reagent for the Treatment of Diseases or Conditions Related to Levels of Vascular Endothelial Growth Factor Receptor

Background Of The Invention

This application is a continuation-in-part of Pavco et al., U.S. Serial No. 60/005,974 all of which is hereby incorporated by reference herein (including drawings).

This invention relates to methods and reagents for the treatment of diseases or conditions relating to the levels of expression of vascular endothelial growth factor (VEGF) receptor(s).

The following is a discussion of relevant art, none of which is admitted to be prior art to the present invention.

VEGF, also referred to as vascular permeability factor (VPF) and vasculotropin, is a potent and highly specific mitogen of vascular endothelial cells (for a review see Ferrara, 1993 Trends Cardiovas. Med. 3, 244; Neufeld et al., 1994 Prog. Growth Factor Res. 5, 89). VEGF induced neovascularization is implicated in various pathological conditions such as tumor angiogenesis, proliferative diabetic retinopathy, hypoxia-induced angiogenesis, rheumatoid arthritis, psoriasis, wound healing and others.

VEGF, an endothelial cell-specific mitogen, is a 34-45 kDa glycoprotein with a wide range of activities that include promotion of angiogenesis, enhancement of vascular-permeability and others. VEGF belongs to the platelet-derived growth factor (PDGF) family of growth factors with approximately 18% homology with the A and B chain of PDGF at the amino acid level. Additionally, VEGF contains the eight conserved cysteine residues common to all growth factors belonging to the PDGF family (Neufeld et al., supra). VEGF protein is believed to exist

2

predominantly as disulfide-linked homodimers; monomers of VEGF have been shown to be inactive (Plouet et al., 1989 EMBO J. 8, 3801).

VEGF exerts its influence on vascular endothelial 5 cells by binding to specific high-affinity cell surface Covalent receptors. cross-linking experiments 125I-labeled VEGF protein have led to the identification of three high molecular weight complexes of 225, 195 and 175 kDa presumed to be VEGF and VEGF receptor complexes (Vaisman et al., 1990 J. Biol. Chem. 265, 19461). Based 10 on these studies VEGF-specific receptors of 180, 150 and 130 kDa molecular mass were predicted. In endothelial cells, receptors of 150 and the 130 kDa have been identi-The VEGF receptors belong to the superfamily of 15 receptor tyrosine kinases (RTKs) characterized by a conserved cytoplasmic catalytic kinase domain and a hydrophylic kinase sequence. The extracellular domains of the VEGF receptors consist of seven immunoglobulin-like domains that are thought to be involved in VEGF binding 20 functions.

The two most abundant and high-affinity receptors of VEGF are flt-1 (fms-like tyrosine kinase) cloned by Shibuya et al., 1990 Oncogene 5, 519 and KDR (kinase-insert-domain-containing receptor) cloned by Terman et al., 1991 Oncogene 6, 1677. The murine homolog of KDR, cloned by Mathews et al., 1991, Proc. Natl. Acad. Sci., USA, 88, 9026, shares 85% amino acid homology with KDR and is termed as flk-1 (fetal liver kinase-1). Recently it has been shown that the high-affinity binding of VEGF to its receptors is modulated by cell surface-associated heparin and heparin-like molecules (Gitay-Goren et al., 1992 J. Biol. Chem. 267, 6093).

VEGF expression has been associated with several pathological states such as tumor angiogenesis, several forms of blindness, rheumatoid arthritis, psoriasis and others. Following is a brief summary of evidence supporting the involvement of VEGF in various diseases:

PCT/US96/17480

10

- 1) Tumor angiogenesis: Increased levels of VEGF gene expression have been reported in vascularized and edemaassociated brain tumors (Berkman et al., 1993 J. Clini. Invest. 91, 153). A more direct demostration of the role 5 of VEGF in tumor angiogenesis was demonstrated by Jim Kim et al., 1993 Nature 362,841 wherein, monoclonal antibodies against VEGF were successfully used to inhibit the growth of rhabdomyosarcoma, glioblastoma multiforme cells in nude Similarly, expression of a dominant negative mutated form of the flt-1 VEGF receptor inhibits vascularization induced by human glioblastoma cells in nude mice (Millauer et al., 1994, Nature 367, 576).
- 2) Ocular diseses: Aiello et al., 1994 New Engl. J. Med. 331, 1480, showed that the ocular fluid, of a majority of patients suffering from diabetic retinopathy and other retinal disorders, contains a high concentration of Miller et al., 1994 Am. J. Pathol. 145, 574, reported elevated levels of VEGF mRNA in patients suffering from retinal ischemia. These observations support a 20 direct role for VEGF in ocular diseases.
- 3) Psoriasis: Detmar et al., 1994 J. Exp. Med. 180, 1141 reported that VEGF and its receptors were overexpressed in psoriatic skin and psoriatic dermal microvessels, suggesting that VEGF plays a significant role in 25 psoriasis.
- Immunohistochemistry and 4) Rheumatoid arthritis: in situ hybridization studies on tissues from the joints of patients suffering from rheumatoid arthritis show an increased level of VEGF and its receptors (Fava et al., 1994 J. Exp. Med. 180, 341). Additionally, Koch et al., 30 1994 J. Immunol. 152, 4149, found that VEGF-specific antibodies were able to significantly reduce the mitogenic activity of synovial tissues from patients suffering from rheumatoid arthritis. These observations support a direct 35 role for VEGF in rheumatoid arthritis.

In addition to the above data on pathological conditions involving excessive angiogenesis, a number of

4

studies have demonstrated that VEGF is both necessary and sufficient for neovascularization. Takashita et al., 1995 J. Clin. Invest. 93, 662, demonstrated that a single injection of VEGF augmented collateral vessel development in a rabbit model of ischemia. VEGF also can induce neovascularization when injected into the cornea. Expression of the VEGF gene in CHO cells is sufficient to confer tumorigenic potential to the cells. Kim et al., supra and Millauer et al., supra used monoclonal antibodies against VEGF or a dominant negative form of flk-1 receptor to inhibit tumor-induced neovascularization.

During development, VEGF and its receptors are associated with regions of new vascular growth (Millauer et al., 1993 Cell 72, 835; Shalaby et al., 1993 J. Clin.

15 Invest. 91, 2235). Furthermore, transgenic mice lacking either of the VEGF receptors are defective in blood vessel formation, infact these mouse do not survive; flk-1 appears to be required for differentiation of endothelial cells, while flt-1 appears to be required at later stages of vessel formation (Shalaby et al., 1995 Nature 376, 62; Fung et al., 1995 Nature 376, 66). Thus, these receptors must be present to properly signal endothelial cells or their precursors to respond to vascularization-promoting stimuli.

All of the conditions listed above, involve extensive vascularization. This hyper-stimulation of endothelial cells may be alleviated by VEGF antagonists. Thus most of the therapeutic efforts for the above conditions have concentrated on finding inhibitors of the VEGF protein.

25

30

Kim et al., 1993 Nature 362, 841 have been successful in inhibiting VEGF-induced tumor growth and angiogenesis in nude mice by treating the mice with VEGF-specific monoclonal antibody.

Koch et al., 1994 J. Immunol. 152, 4149 showed that 35 the mitogenic activity of microvascular endothelial cells found in rheumatoid arthritis (RA) synovial tissue explants and the chemotactic property of endothelial cells

5

from RA synovial fluid can be neutralized significantly by treatment with VEGF-specific antibodies.

Ullrich et al., International PCT Publication No. WO 94/11499 and Millauer et al., 1994 Nature 367, 576 used a soluble form of flk-1 receptor (dominant-negative mutant) to prevent VEGF-mediated tumor angiogenesis in immunodeficient mice.

Kendall and Thomas, International PCT Publication No. WO 94/21679 describe the use of naturally occuring or recombinantly-engineered soluble forms of VEGF receptors to inhibit VEGF activity.

Robinson, International PCT Publication No. WO 95/04142 describes the use of antisense oligonucleotides targeted against VEGF RNA to inhibit VEGF expression.

Jellinek et al., 1994 Biochemistry 33, 10450 describe the use of VEGF-specific high-affinity RNA aptamers to inhibit the binding of VEGF to its receptors.

Rockwell and Goldstein, International PCT Publication No. WO 95/21868, describe the use of anti-VEGF receptor monoclonal antibodies to neutralize the the effect of VEGF on endothelial cells.

Summary Of The Invention

15

25

30

The invention features novel nucleic acid-based techniques [e.g., enzymatic nucleic acid molecules (ribozymes), antisense nucleic acids, 2-5A antisense chimeras, triplex DNA, antisense nucleic acids containing RNA cleaving chemical groups (Cook et al., U.S. Patent 5,359,051)] and methods for their use to down regulate or inhibit the expression of receptors of VEGF (VEGF-R).

In a preferred embodiment, the invention features use of one or more of the nucleic acid-based techniques to inhibit the expression of flt-1 and/or flk-1/KDR receptors.

By "inhibit" it is meant that the activity of VEGF-R or level of mRNAs or equivalent RNAs encoding VEGF-R is reduced below that observed in the absence of the nucleic acid. In one embodiment, inhibition with ribozymes

6

preferably is below that level observed in the presence of an enzymatically inactive RNA molecule that is able to bind to the same site on the mRNA, but is unable to cleave that RNA. In another embodiment, inhibition with antisense oligonucleotides is preferably below that level observed in the presence of for example, an oligonucleotide with scrambled sequence or with mismatches.

By "enzymatic nucleic acid molecule" it is meant an RNA molecule which has complementarity in a substrate binding region to a specified gene target, and also has an enzymatic activity which is active to specifically cleave target RNA. That is, the enzymatic RNA molecule is able to intermolecularly cleave RNA and thereby inactivate a target RNA molecule. This complementary regions allow sufficient hybridization of the enzymatic RNA molecule to the target RNA and thus permit cleavage. One hundred percent complementarity is preferred, but complementarity as low as 50-75% may also be useful in this invention. By "equivalent" RNA to VEGF-R is meant to include those naturally occurring RNA molecules in various animals, including human, mice, rats, rabbits, primates and pigs.

By "antisense nucleic acid" it is meant a nonenzymatic nucleic acid molecule that binds to target RNA by means of RNA-RNA or RNA-DNA or RNA-PNA (protein nucleic 25 acid; Egholm et al., 1993 Nature 365, 566) interactions and alters the activity of the target RNA (for a review see Stein and Cheng, 1993 Science 261, 1004).

By "2-5A antisense chimera" it is meant, an antisense oligonucleotide containing a 5' phosphorylated 2'-5'-30 linked adenylate residues. These chimeras bind to target RNA in a sequence-specific manner and activate a cellular 2-5A-dependent ribonuclease which, in turn, cleaves the target RNA (Torrence et al., 1993 Proc. Natl. Acad. Sci. USA 90, 1300).

35 By "triplex DNA" it is meant an oligonucleotide that can bind to a double-stranded DNA in a sequence-specific manner to form a triple-strand helix. Formation of such

7

triple helix structure has been shown to inhibit transcription of the targeted gene (Duval-Valentin et al., 1992 Proc. Natl. Acad. Sci. USA 89, 504).

By "gene" it is meant a nucleic acid that encodes an 5 RNA.

By "complementarity" it is meant a nucleic acid that can form hydrogen bond(s) with other RNA sequence by either traditional Watson-Crick or other non-traditional types (for example, Hoogsteen type) of base-paired interactions.

10

Six basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds in trans (and thus can cleave other RNA molecules) under physiological condi-15 tions. Table I summarizes some of the characteristics of these ribozymes. In general, enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs through the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary baseand once bound to the correct site, pairing, enzymatically to cut the target RNA. Strategic cleavage 25 of such a target RNA will destroy its ability to direct synthesis of an encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets. single ribozyme molecule is able to cleave many molecules In addition, the ribozyme is a highly of target RNA. specific inhibitor of gene expression, with the specificity of inhibition depending not only on the base-pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can completely eliminate catalytic activity of a ribozyme.

8

Ribozymes that cleave the specified sites in VEGF-R mRNAs represent a novel therapeutic approach to treat tumor angiogenesis, ocular diseases, rhuematoid arthritis, psoriasis and others. Applicant indicates that ribozymes are able to inhibit the activity of VEGF-R (specifically flt-1 and flk-1/KDR) and that the catalytic activity of the ribozymes is required for their inhibitory effect. Those of ordinary skill in the art will find that it is clear from the examples described that other ribozymes that cleave VEGF-R mRNAs may be readily designed and are within the invention.

In preferred embodiments of this invention, the enzymatic nucleic acid molecule is formed in a hammerhead or hairpin motif, but may also be formed in the motif of a hepatitis delta virus, group I intron or RNaseP RNA (in 15 association with an RNA guide sequence) or Neurospora VS RNA. Examples of such hammerhead motifs are described by Rossi et al., 1992, AIDS Research and Human Retroviruses 8, 183, of hairpin motifs by Hampel et al., EP0360257, Hampel and Tritz, 1989 Biochemistry 28, 4929, and Hampel 20 et al., 1990 Nucleic Acids Res. 18, 299, and an example of the hepatitis delta virus motif is described by Perrotta and Been, 1992 Biochemistry 31, 16; of the RNaseP motif by Guerrier-Takada et al., 1983 Cell 35, 849, Neurospora VS RNA ribozyme motif is described by Collins (Saville and Collins, 1990 Cell 61, 685-696; Saville and Collins, 1991 Proc. Natl. Acad. Sci. USA 88, 8826-8830; Collins and Olive, 1993 Biochemistry 32, 2795-2799) and of the Group I intron by Cech et al., U.S. Patent 4,987,071. 30 specific motifs are not limiting in the invention and those skilled in the art will recognize that all that is important in an enzymatic nucleic acid molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene 35 RNA regions, and that it have nucleotide sequences within or surrounding that substrate binding site which impart an RNA cleaving activity to the molecule.

9

In a preferred embodiment the invention provides a method for producing a class of enzymatic cleaving agents which exhibit a high degree of specificity for the RNA of a desired target. The enzymatic nucleic acid molecule is preferably targeted to a highly conserved sequence region of target mRNAs encoding VEGF-R proteins (specifically flt-1 and flk-1/KDR) such that specific treatment of a disease or condition can be provided with either one or several enzymatic nucleic acids. Such enzymatic nucleic acid molecules can be delivered exogenously to specific tissue or cellular targets as required. Alternatively, the ribozymes can be expressed from DNA and/or RNA vectors that are delivered to specific cells.

Synthesis of nucleic acids greater than 100 nucleo-15 tides in length is difficult using automated methods, and the therapeutic cost of such molecules is prohibitive. In this invention, small nucleic acid motifs (e.g., antisense oligonucleotides, hammerhead or the hairpin ribozymes) are used for exogenous delivery. The simple structure of 20 these molecules increases the ability of the nucleic acid to invade targeted regions of the mRNA structure. However, these nucleic acid molecules can also be expressed within cells from eukaryotic promoters (e.g., Izant and Weintraub, 1985 Science 229, 345; McGarry and 25 Lindquist, 1986 Proc. Natl. Acad. Sci. USA 83, 399; Sullenger-Scanlon et al., 1991, Proc. Natl. Acad. Sci. USA, 88, 10591-5; Kashani-Sabet et al., 1992 Antisense Res. Dev., 2, 3-15; Dropulic et al., 1992 J. Virol, 66, 1432-41; Weerasinghe et al., 1991 J. Virol, 65, 5531-4; 30 Ojwang et al., 1992 Proc. Natl. Acad. Sci. USA 89, 10802-6; Chen et al., 1992 Nucleic Acids Res., 20, 4581-9; Sarver et al., 1990 Science 247, 1222-1225; Thompson et al., 1995 Nucleic Acids Res. 23, 2259). Those skilled in the art realize that any nucleic acid can be expressed in 35 eukaryotic cells from the appropriate DNA/RNA vector. The activity of such nucleic acids can be augmented by their release from the primary transcript by a ribozyme (Draper

et al., PCT W093/23569, and Sullivan et al., PCT W094/02595, both hereby incorporated in their totality by reference herein; Ohkawa et al., 1992 Nucleic Acids Symp. Ser., 27, 15-6; Taira et al., 1991, Nucleic Acids Res., 19, 5125-30; Ventura et al., 1993 Nucleic Acids Res., 21, 3249-55; Chowrira et al., 1994 J. Biol. Chem. 269, 25856).

Such nucleic acids are useful for the prevention of the diseases and conditions discussed above, and any other diseases or conditions that are related to the levels of VEGF-R (specifically flt-1 and flk-1/KDR) in a cell or tissue.

By "related" is meant that the reduction of VEGF-R (specifically flt-1 and flk-1/KDR) RNA levels and thus reduction in the level of the respective protein will relieve, to some extent, the symptoms of the disease or condition.

Ribozymes are added directly, or can be complexed with cationic lipids, packaged within liposomes, or otherwise delivered to target cells or tissues. The nucleic 20 acid or nucleic acid complexes can be locally administered to relevant tissues ex vivo, or in vivo through injection, infusion pump or stent, with or without their incorpora-In preferred embodiments, the tion in biopolymers. ribozymes have binding arms which are complementary to the 25 sequences in Tables II to IX. Examples of such ribozymes also are shown in Tables II to IX. Examples of such ribozymes consist essentially of sequences defined in these By "consists essentially of" is meant that the active ribozyme contains an enzymatic center equivalent to 30 those in the examples, and binding arms able to bind mRNA such that cleavage at the target site occurs. sequences may be present which do not interfere with such cleavage.

In another aspect of the invention, ribozymes that cleave target RNA molecules and inhibit VEGF-R (specifically flt-1 and flk-1/KDR) activity are expressed from transcription units inserted into DNA or RNA vectors. The

11

recombinant vectors are preferably DNA plasmids or viral vectors. Ribozyme expressing viral vectors could be constructed based on, but not limited to, adeno-associated virus, retrovirus, adenovirus, or alphavirus. Preferably, 5 the recombinant vectors capable of expressing the ribozymes are delivered as described above, and persist in target cells. Alternatively, viral vectors may be used that provide for transient expression of ribozymes. vectors might be repeatedly administered as necessary. 10 Once expressed, the ribozymes cleave the target mRNA. Delivery of ribozyme expressing vectors could be systemic, such as by intravenous or intramuscular administration, by administration to target cells ex-planted from the patient followed by reintroduction into the patient, or by any 15 other means that would allow for introduction into the desired target cell.

By "vectors" is meant any nucleic acid- and/or viralbased technique used to deliver a desired nucleic acid.

Other features and advantages of the invention will 20 be apparent from the following description of the preferred embodiments thereof, and from the claims.

Description Of The Preferred Embodiments

First the drawings will be described briefly.

Drawings

25 Figure 1 is a diagrammatic representation of the hammerhead ribozyme domain known in the art. Stem II can be ≥ 2 base-pair long.

Figure 2a is a diagrammatic representation of the hammerhead ribozyme domain known in the art; Figure 2b is a diagrammatic representation of the hammerhead ribozyme as divided by Uhlenbeck (1987, Nature, 327, 596-600) into a substrate and enzyme portion; Figure 2c is a similar diagram showing the hammerhead divided by Haseloff and Gerlach (1988, Nature, 334, 585-591) into two portions; and Figure 2d is a similar diagram showing the hammerhead

divided by Jeffries and Symons (1989, Nucl. Acids. Res., 17, 1371-1371) into two portions.

Figure 3 is a diagramatic representation of the general structure of a hairpin ribozyme. Helix 2 (H2) is 5 provided with a least 4 base pairs (i.e., n is 1, 2, 3 or 4) and helix 5 can be optionally provided of length 2 or more bases (preferably 3 - 20 bases, i.e., m is from 1 -20 or more). Helix 2 and helix 5 may be covalently linked by one or more bases (i.e., r is ≥ 1 base). Helix 1, 4 or 5 may also be extended by 2 or more base pairs (e.g., 4 -20 base pairs) to stabilize the ribozyme structure, and preferably is a protein binding site. In each instance, each N and N' independently is any normal or modified base and each dash represents a potential base-pairing inter-15 action. These nucleotides may be modified at the sugar, base or phosphate. Complete base-pairing is not required in the helices, but is preferred. Helix 1 and 4 can be of any size (i.e., o and p is each independently from 0 to any number, e.g., 20) as long as some base-pairing is 20 maintained. Essential bases are shown as specific bases in the structure, but those in the art will recognize that one or more may be modified chemically (abasic, base, sugar and/or phosphate modifications) or replaced with another base without significant effect. Helix 4 can be 25 formed from two separate molecules, i.e., without a connecting loop. The connecting loop when present may be a ribonucleotide with or without modifications to its base, sugar or phosphate. "q" is ≥ 2 bases. The connecting loop can also be replaced with a non-nucleotide linker H refers to bases A, U, or C. 30 molecule. pyrimidine bases. " " refers to a covalent bond.

Figure 4 is a representation of the general structure of the hepatitis delta virus ribozyme domain known in the art.

35 Figure 5 is a representation of the general structure of the VS RNA ribozyme domain.

13

Figure 6 is a schematic representation of an RNAseH Specifically, the left side of accessibility assay. Figure 6 is a diagram of complementary DNA oligonucleotides bound to accessible sites on the target RNA. 5 Complementary DNA oligonucleotides are represented by broad lines labeled A, B, and C. Target RNA is represented by the thin, twisted line. The right side of Figure 6 is a schematic of a gel separation of uncut target RNA from a cleaved target RNA. Detection of target RNA is by autoradiography of body-labeled, T7 transcript. The bands common to each lane represent uncleaved target RNA; the bands unique to each lane represent the cleaved products.

Figure 7 shows the effect of hammerhead ribozymes targeted against flt-1 receptor on the binding of VEGF to 15 the surface of human microvascular endothelial cells. Sequences of the ribozymes used are shown in Table II; the length of stem II region is 3 bp. The hammerhead ribozymes were chemically modified such that the ribozyme 20 consists of ribose residues at five positions (see Figure 11); U4 and U7 positions contain 2'-NH, modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions; four nucleotides at the 5' terminus contains phosphorothicate substitutions. Additionally, the 3' end 25 of the ribozyme contains a 3'-3' linked inverted abasic deoxyribose. The results of two separate experiments are shown as separate bars for each set. Each bar represents the average of triplicate samples. The standard deviation is shown with error bars. For the flt-1 data, 500 nM ribozyme (3:1 charge ratio with LipofectAMINE®) was used. 30 Control 1-10 is the control for ribozymes 307-2797, control 11-20 is the control for ribozymes 3008-5585. The Control 1-10 and Control 11-20 represent the treatment of cells with LipofectAMINE® alone without any ribozymes.

Figure 8 shows the effect of hammerhead ribozymes targeted against KDR receptor on the binding of VEGF to KDR on the surface of human microvascular endothelial

35

PCT/US96/17480 WO 97/15662

14

cells. Sequences of the ribozymes used are shown in Table IV; the length of stem II region is 3 bp. The hammerhead ribozymes were chemically modified such that the ribozyme consists of ribose residues at five positions (see Figure 5 11); U4 and U7 positions contain 2'-NH, modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions; four nucleotides at the 5' terminus contains phosphorothicate substitutions. Additionally, the 3' end of the ribozyme contains a 3'-3' linked inverted abasic 10 deoxyribose. The Control 1-10 and Control 11-20 represent the treatment of cells with LipofectAMINE® alone without any ribozymes. Irrel. RZ, is a control experiment wherein the cells are treated with a non-KDR-targeted ribozyme complexed with Lipofectamine®. 200 nM ribozyme (3:1 15 charge ratio with LipofectAMINE®) was used. In addition to the KDR-targeted ribozymes, the effect on VEGF binding of a ribozyme targeted to an irrelevant mRNA (irrel. RZ) Because the affinity of KDR for VEGF is is also shown. about 10-fold lower than the affinity of flt-1 for VEGF, a higher concentration of VEGF was used in the binding assay.

Figure 9 shows the specificity of hammerhead ribozymes targeted against flt-1 receptor. Inhibition of the binding of VEGF, urokinase plasminogen activator (UPA) and 25 fibroblast growth factor (FGF) to their corresponding receptors as a function of anti-FLT ribozymes is shown. The sequence and description of the ribozymes used are as described under Figure 7 above. The average of triplicate samples is given; percent inhibition as calculated below.

20

30

Figure 10 shows the inhibition of the proliferation of Human aortic endothelial cells (HAEC) mediated by phosphorothicate antisense oligodeoxynucleotides targeted against human KDR receptor RNA. Cell proliferation (O.D. 490) as a function of antisense oligodeoxynucleotide 35 concentration is shown. KDR 21AS represents a 21 nt phosphorothicate antisense oligodeoxynucleotide targeted KDR 21 Scram represents a 21 nt against KDR RNA.

15

phosphorothicate oligodeoxynucleotide having a scrambled sequence. LF represents the lipid carrier Lipofectin.

Figure 11 shows in vitro cleavage of flt-1 RNA by hammerhead ribozymes. A) diagrammatic representation of 5 hammerhead ribozymes targeted against flt-1 RNA. hammerhead (HH) ribozymes were chemically modified such that the ribozyme consists of ribose residues at five positions; U4 and U7 positions contain 2'-NH, modificathe remaining nucleotide positions contain tions, 10 2'-O-methyl substitutions; four nucleotides at the 5' phosphorothioate contains substitutions. terminus Additionally, the 3' end of the ribozyme contains a 3'-3' linked inverted abasic deoxyribose (designated as 3'-iH). 1358 HH-A and 4229 HH-A contain 3 base-paired stem II 1358 HH-B and 4229 HH-B contain 4 base-paired 15 region. stem II region. B) and C) shows in vitro cleavage kinetics of HH ribozymes targeted against sites 1358 and 4229 within the flt-1 RNA.

Figure 12 shows inhibition of human microvascular 20 endothelial cell proliferation mediated by anti-flt-1 hammerhead ribozymes. A) Diagrammatic representation of hammerhead (HH) ribozymes targeted against sites 1358 and 4229 within the the flt-1 RNA. B) Graphical representation of the inhibition of cell proliferation mediated by 1358HH and 4229HH ribozymes.

Figure 13 shows inhibition of human microvascular endothelial cell proliferation mediated by anti-KDR hammerhead ribozymes. The figure is a graphical representation of the inhibition of cell proliferation mediated by hammerhead ribozymes targeted against sites 527, 730, 3702 and 3950 within the KDR RNA. Irrelevant HH RZ is a hammerhead ribozyme targeted to an irrelevant target. All of these ribozymes, including the Irrelevant HH RZ, were chemically modified such that the ribozyme consists of ribose residues at five positions; U4 and U7 positions contain 2'-NH₂ modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions; four

PCT/US96/17480 WO 97/15662

nucleotides at the 5' termini contain phosphorothioate Additionally, the 3' end of the ribozyme substitutions. contains a 3'-3' linked inverted abasic deoxyribose (3'-iH).

5

Figure 14 shows in vitro cleavage of KDR RNA by hammerhead ribozymes. The hammerhead (HH) ribozymes were chemically modified such that the ribozyme consists of ribose residues at five positions; U4 and U7 positions contain 2'-NH, modifications, the remaining nucleotide 10 positions contain 2'-O-methyl substitutions. ally, the 3' end of the ribozyme contains a 3'-3' linked inverted abasic deoxyribose (designated as 3'-iH). and 527 HH contain 4 base-paired stem II region. Percent in vitro cleavage kinetics as a function of time of HH ribozymes targeted against sites 527 and 726 within the KDR RNA is shown.

Figure 15 shows in vitro cleavage of KDR RNA by hammerhead ribozymes. The hammerhead (HH) ribozymes were chemically modified such that the ribozyme consists of 20 ribose residues at five positions; U4 and U7 positions contain 2'-NH, modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions. ally, the 3' end of the ribozyme contains a 3'-3' linked inverted abasic deoxyribose (designated as 3'-iH). 25 HH and 3950 HH contain 4 base-paired stem II region. Percentin vitro cleavage kinetics as a function of time of HH ribozymes targeted against sites 3702 and 3950 within the KDR RNA is shown.

Figure 16 shows in vitro cleavage of RNA by hammer-30 head ribozymes that are targeted to sites that are conserved between flt-1 and KDR RNA. The hammerhead (HH) ribozymes were chemically modified such that the ribozyme consists of ribose residues at five positions; U4 and U7 positions contain 2'-NH2 modifications, the remaining 35 nucleotide positions contain 2'-O-methyl substitutions. Additionally, the 3' end of the ribozyme contains a 3'-3' linked inverted abasic deoxyribose (designated as 3'-iH).

17

FLT/KDR-I HH ribozyme was synthesized with either a 4 base-paired or a 3 base-paired stem II region. FLT/KDR-I HH can cleave site 3388 within flt-1 RNA and site 3151 within KDR RNA. Percent in vitro cleavage kinetics as a function of time of HH ribozymes targeted against sites 3702 and 3950 within the KDR RNA is shown.

Figure 17 shows inhibition of human microvascular endothelial cell proliferation mediated by anti-KDR and anti-flt-1 hammerhead ribozymes. The figure is a graph-10 ical representation of the inhibition of cell proliferation mediated by hammerhead ribozymes targeted against sites KDR sites-527, 726 or 3950 or flt-1 site 4229. figure also shows enhanced inhibition of cell proliferation by a combination of flt-1 and KDR hammerhead ribo-4229+527, indicates the treatment of cells with 15 zymes. both the flt 4229 and the KDR 527 ribozymes. indicates the treatment of cells with both the flt 4229 and the KDR 726 ribozymes. 4229+3950, indicates the treatment of cells with both the flt 4229 and the KDR 3950 VEGF -, indicates the basal level of cell 20 ribozymes. proliferation in the absence of VEGF. A, indicates catalytically active ribozyme; I, indicates catalytically inactive ribozyme. All of these ribozymes were chemically modified such that the ribozyme consists of ribose 25 residues at five positions; U4 and U7 positions contain 2'-NH, modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions; four nucleotides at the termini contain phosphorothicate substitutions. Additionally, the 3' end of the ribozyme contains a 3'-3' 30 linked inverted abasic deoxyribose (3'-iH).

Figure 18 shows the inhibition of VEGF-induced angiogenesis in rat cornea mediated by anti-flt-1 hammerhead ribozyme. All of these ribozymes were chemically modified such that the ribozyme consists of ribose residues at five positions; U4 position contains 2'-C-allyl modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions; four nucleotides at the 5' termini contain

18

phosphorothicate substitutions. Additionally, the 3' end of the ribozyme contains a 3'-3' linked inverted abasic deoxyribose (3'-iH). A decrease in the Surface Area corresponds to a reduction in angiogenesis. VEGF alone, 5 corresponds to treatment of the cornea with VEGF and no Vehicle alone, corresponds to the treatment ribozymes. of the cornea with the carrier alone and no VEGF. This control gives a basal level of Surface Area. Active 4229 HH, corresponds to the treatment of cornea with the flt-1 10 4229 HH ribozyme in the absence of any VEGF. This control also gives a basal level of Surface Area. Active 4229 HH + VEGF, corresponds to the co-treatment of cornea with the flt-1 4229 HH ribozyme and VEGF. Inactive 4229 HH + VEGF, corresponds to the co-treatment of cornea with a catalytically inactive version of 4229 HH ribozyme and VEGF.

Ribozymes

Ribozymes of this invention block to some extent VEGF-R (specifically flt-1 and flk-1/KDR) production and can be used to treat disease or diagnose such disease.

20 Ribozymes will be delivered to cells in culture, to cells or tissues in animal models of angiogenesis and/or RA and to human cells or tissues ex vivo or in vivo. Ribozyme cleavage of VEGF-R RNAs (specifically RNAs that encode flt-1 and flk-1/KDR) in these systems may alleviate disease symptoms.

Target sites

Targets for useful ribozymes can be determined as disclosed in Draper et al., International PCT Publication No. WO 95/13380, and hereby incorporated by reference herein in totality. Other examples include the following PCT applications which concern inactivation of expression of disease-related genes: WO 95/23225, WO 95/13380, WO 94/02595, incorporated by reference herein. Rather than repeat the guidance provided in those documents here, below are provided specific examples of such methods, not

19

limiting to those in the art. Ribozymes to such targets are designed as described in those applications and synthesized to be tested in vitro and in vivo, as also described.

The sequence of human and mouse flt-1, KDR and/or 5 flk-1 mRNAs were screened for optimal ribozyme target sites using a computer folding algorithm. Hammerhead or hairpin ribozyme cleavage sites were identified. sites are shown in Tables II to IX (all sequences are 5' to 3' in the tables; X can be any base-paired sequence, 10 the actual sequence is not relevant here). The nucleotide base position is noted in the Tables as that site to be cleaved by the designated type of ribozyme. While mouse and human sequences can be screened and ribozymes there-15 after designed, the human targeted sequences are of most However, as discussed in Stinchcomb et al., utility. "Method and Composition for Treatment of Restenosis and Cancer Using Ribozymes," filed May 18, 1994, U.S.S.N. 08/245,466, mouse targeted ribozymes may be useful to test 20 efficacy of action of the ribozyme prior to testing in The nucleotide base position is noted in the Tables as that site to be cleaved by the designated type of ribozyme.

Hammerhead or hairpin ribozymes were designed that could bind and cleave target RNA in a sequence-specific manner. The ribozymes were individually analyzed by computer folding (Jaeger et al., 1989 Proc. Natl. Acad. Sci. USA, 86, 7706) to assess whether the ribozyme sequences fold into the appropriate secondary structure.

Those ribozymes with unfavorable intramolecular interactions between the binding arms and the catalytic core were eliminated from consideration. Varying binding arm lengths can be chosen to optimize activity.

Referring to Figure 6, mRNA is screened for access-35 ible cleavage sites by the method described generally in Draper et al., PCT WO93/23569, hereby incorporated by reference herein. Briefly, DNA oligonucleotides

complementary to potential hammerhead or hairpin ribozyme cleavage sites were synthesized. A polymerase chain reaction is used to generate substrates for T7 polymerase transcription from human and mouse flt-1, KDR and/or flk-1 cDNA clones. Labeled RNA transcripts are synthesized in vitro from the templates. The oligonucleotides and the labeled transcripts were annealed, RNAseH was added and the mixtures were incubated for the designated times at 37°C. Reactions are stopped and RNA separated on sequencing polyacrylamide gels. The percentage of the substrate cleaved is determined by autoradiographic quantitation using a PhosphorImaging system. From these data, hammerhead or hairpin ribozyme sites are chosen as the most accessible.

Ribozymes of the hammerhead or hairpin motif were 15 designed to anneal to various sites in the mRNA message. The binding arms are complementary to the target site sequences described above. The ribozymes were chemically synthesized. The method of synthesis used follows the 20 procedure for normal RNA synthesis as described in Usman et al., 1987 J. Am. Chem. Soc., 109, 7845; Scaringe et al., 1990 Nucleic Acids Res., 18, 5433; and Wincott et al., 1995 Nucleic Acids Res. 23, 2677-2684 and makes use of common nucleic acid protecting and coupling groups, such as dimethoxytrityl at the 5'-end, and phosphoramidites at the 3'-end. Small scale synthesis were conducted on a 394 Applied Biosystems, Inc. synthesizer using a modified 2.5 μ mol scale protocol with a 5 min coupling step for alkylsilyl protected nucleotides and 2.5 30 min coupling step for 2'-O-methylated nucleotides. Table XI outlines the amounts, and the contact times, of the reagents used in the synthesis cycle. A 6.5-fold excess (163 μ L of 0.1 M = 16.3 μ mol) of phosphoramidite and a 24-fold excess of S-ethyl tetrazole (238 μ L of 0.25 M = 59.5 μmol) relative to polymer-bound 5'-hydroxyl was used 35 in each coupling cycle. Average coupling yields on the 394 Applied Biosystems, Inc. synthesizer, determined by

10

30

colorimetric quantitation of the trityl fractions, were 97.5-99%. Other oligonucleotide synthesis reagents for the 394 Applied Biosystems, Inc. synthesizer: detritylation solution was 2% TCA in methylene chloride (ABI); capping 5 was performed with 16% N-methyl imidazole in THF (ABI) and 10% acetic anhydride/10% 2,6-lutidine in THF oxidation solution was 16.9 mM I2, 49 mM pyridine, 9% water in THF (Millipore). B & J Synthesis Grade acetonitrile was used directly from the reagent bottle. S-Ethyl tetrazole solution (0.25 M in acetonitrile) was made up from the solid obtained from American International Chemical, Inc.

Deprotection of the RNA was performed as follows. The polymer-bound oligoribonucleotide, trityl-off, was transferred from the synthesis column to a 4mL glass screw top vial and suspended in a solution of methylamine (MA) at 65 *C for 10 min. After cooling to -20 *C, the supernatant was removed from the polymer support. The support was washed three times with 1.0 mL of EtOH: MeCN: H2O/3:1:1, 20 vortexed and the supernatant was then added to the first supernatant. The combined supernatants, containing the oligoribonucleotide, were dried to a white powder.

The base-deprotected oligoribonucleotide was resuspended in anhydrous TEA \bullet HF/NMP solution (250 μ L of a solution of 1.5mL N-methylpyrrolidinone, 750 µL TEA and 1.0 mL TEA•3HF to provide a 1.4M HF concentration) and heated to 65°C for 1.5 h. The resulting, fully deprotected, oligomer was quenched with 50 mM TEAB (9 mL) prior to anion exchange desalting.

For anion exchange desalting of the deprotected oligomer, the TEAB solution was loaded onto a Qiagen 500® anion exchange cartridge (Qiagen Inc.) that was prewashed with 50 mM TEAB (10 mL). After washing the loaded cartridge with 50 mM TEAB (10 mL), the RNA was eluted with 2 M TEAB (10 mL) and dried down to a white powder.

Inactive hammerhead ribozymes were synthesized by substituting a U for G_5 and a U for A_{14} (numbering from 10

Hertel, K. J., et al., 1992, <u>Nucleic Acids Res.</u>, 20, 3252).

The average stepwise coupling yields were >98% (Wincott et al., 1995 Nucleic Acids Res. 23, 2677-2684).

Hairpin ribozymes are synthesized in two parts and annealed to reconstruct the active ribozyme (Chowrira and Burke, 1992 Nucleic Acids Res., 20, 2835-2840). Ribozymes are also synthesized from DNA templates using bacteriophage T7 RNA polymerase (Milligan and Uhlenbeck, 1989, Methods Enzymol. 180, 51).

All ribozymes are modified extensively to enhance stability by modification with nuclease resistant groups, for example, 2'-amino, 2'-C-allyl, 2'-flouro, 2'-O-methyl, 2'-H (for a review see Usman and Cedergren, 1992 TIBS 17, 34; Usman et al., 1994 Nucleic Acids Symp. Ser. 31, 163). Ribozymes are purified by gel electrophoresis using general methods or are purified by high pressure liquid chromatography (HPLC; See Usman et al., PCT Publication No. WO95/23225, the totality of which is hereby incorporated herein by reference) and are resuspended in water.

The sequences of the ribozymes that are chemically synthesized, useful in this study, are shown in Tables II Those in the art will recognize that these to IX. sequences are representative only of many more such 25 sequences where the enzymatic portion of the ribozyme (all but the binding arms) is altered to affect activity. Stem-loop IV sequence of hairpin ribozymes listed in for (5'-CACGUUGUG-3') can be altered example Table III (substitution, deletion, and/or insertion) to contain any 30 sequence, provided a minimum of two base-paired stem structure can form. The sequences listed in Tables II to IX may be formed of ribonucleotides or other nucleotides or non-nucleotides. Such ribozymes are equivalent to the ribozymes described specifically in the Tables.

Optimizing Ribozyme Activity

Ribozyme activity can be optimized as described by Stinchcomb et al., supra. The details will not be repeated here, but include altering the length of the 5 ribozyme binding arms (stems I and III, see Figure 2c), or chemically synthesizing ribozymes with modifications that prevent their degradation by serum ribonucleases (see e.g., Eckstein et al., International Publication No. WO 92/07065; Perrault et al., 1990 Nature 344, 565; Pieken et 10 al., 1991 Science 253, 314; Usman and Cedergren, 1992 Trends in Biochem. Sci. 17, 334; Usman et al., International Publication No. WO 93/15187; Rossi International Publication No. WO 91/03162; Beigelman et al., 1995 J. Biol Chem. in press; as well as Sproat, US 15 Patent No. 5,334,711 which describe various chemical modifications that can be made to the sugar moieties of enzymatic RNA molecules). Modifications which enhance their efficacy in cells, and removal of stem II bases to shorten RNA synthesis times and reduce chemical require-20 ments are desired. (All these publications are hereby incorporated by reference herein).

Sullivan, et al., supra, describes the general delivery of enzymatic RNA molecules. methods for Ribozymes may be administered to cells by a variety of 25 methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres. For some indications, ribozymes 30 may be directly delivered ex vivo to cells or tissues with or without the aforementioned vehicles. Alternatively, the RNA/vehicle combination is locally delivered by direct injection or by use of a catheter, infusion pump or stent. Other routes of delivery include, but are not limited to. 35 intravascular, intramuscular, subcutaneous or joint injection, aerosol inhalation, oral (tablet or pill form), topical, systemic, ocular, intraperitoneal and/or intrathecal delivery. More detailed descriptions of ribozyme delivery and administration are provided in Sullivan et al., supra and Draper et al., supra which have been incorporated by reference herein.

Another means of accumulating high concentrations of 5 a ribozyme(s) within cells is to incorporate the ribozymeencoding sequences into a DNA or RNA expression vector. Transcription of the ribozyme sequences are driven from a promoter for eukaryotic RNA polymerase I (pol I), RNA 10 polymerase II (pol II), or RNA polymerase III (pol III). Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, 15 silencers, etc.) present nearby. Prokaryotic RNA polymerase promoters are also used, providing that the prokaryotic RNA polymerase enzyme is expressed in the appropriate cells (Elroy-Stein and Moss, 1990 Proc. Natl. Acad. Sci. U S A, 87, 6743-7; Gao and Huang 1993 Nucleic Acids Res., 20 21, 2867-72; Lieber et al., 1993 Methods Enzymol., 47-66; Zhou et al., 1990 Mol. Cell. Biol., 10, 4529-37; Thompson et al., 1995 supra). Several investigators have demonstrated that ribozymes expressed from such promoters can function in mammalian cells (e.g. Kashani-Sabet et 25 al., 1992 Antisense Res. Dev., 2, 3-15; Ojwang et al., 1992 Proc. Natl. Acad. Sci. U S A, 89, 10802-6; Chen et al., 1992 Nucleic Acids Res., 20, 4581-9; Yu et al., 1993 Proc. Natl. Acad. Sci. U S A, 90, 6340-4; L'Huillier et al., 1992 EMBO J. 11, 4411-8; Lisziewicz et al., 1993 30 Proc. Natl. Acad. Sci. U. S. A., 90, 8000-4; Thompson et al., 1995 Nucleic Acids Res. 23, 2259). The above ribozyme transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, 35 viral DNA vectors (such as adenovirus or adeno-associated virus vectors), or viral RNA vectors (such as retroviral or alphavirus vectors).

preferred embodiment of the invention, a transcription unit expressing a ribozyme that cleaves RNAs that encode flt-1, KDR and/or flk-1 are inserted into a plasmid DNA vector or an adenovirus or adeno-associated 5 virus DNA viral vector or a retroviral RNA vector. Viral vectors have been used to transfer genes and lead to either transient or long term gene expression (Zabner et al., 1993 Cell 75, 207; Carter, 1992 Curr. Opi. Biotech. 3. 533). The adenovirus, AAV or retroviral vector is delivered as recombinant viral particles. The DNA may be delivered alone or complexed with vehicles (as described for RNA above). The recombinant adenovirus or AAV or retroviral particles are locally administered to the site of treatment, e.q., through incubation or inhalation in vivo or by direct application to cells or tissues ex Retroviral vectors have also been used to express ribozymes in mammalian cells (Ojwang et al., 1992 supra; Thompson et al., 1995 supra).

acid-based therapeutic targets by several criteria. The interaction between VEGF and VEGF-R is well-established. Efficacy can be tested in well-defined and predictive animal models. Finally, the disease conditions are serious and current therapies are inadequate. Whereas protein-based therapies would inhibit VEGF activity nucleic acid-based therapy provides a direct and elegant approach to directly modulate flt-1, KDR and/or flk-1 expression.

Because flt-1 and KDR mRNAs are highly homologous in certain regions, some ribozyme target sites are also homologous (see Table X). In this case, a single ribozyme will target both flt-1 and KDR mRNAs. At partially homologous sites, a single ribozyme can sometimes be designed to accomodate a site on both mRNAs by including G/U basepairing. For example, if there is a G present in a ribozyme target site in KDR mRNA at the same position there is an A in the flt-1 ribozyme target site, the

ribozyme can be synthesized with a U at the complementary position and it will bind both to sites. The advantage of one ribozyme that targets both VEGF-R mRNAs is clear, especially in cases where both VEGF receptors may con-5 tribute to the progression of angiogenesis in the disease state.

"Angiogenesis" refers to formation of new blood vessels which is an essential process in reproduction, development and wound repair. "Tumor angiogenesis" refers 10 to the induction of the growth of blood vessels from surrounding tissue into a solid tumor. Tumor growth and tumor metastasis are dependent on angiogenesis (for a review see Folkman, 1985 supra; Folkman 1990 J. Natl. Cancer Inst., 82, 4; Folkman and Shing, 1992 J. Biol. 15 Chem. 267, 10931).

Angiogenesis plays an important role in diseases such as arthritis wherein new blood vessels have been shown to invade the joints and degrade cartilage (Folkman and Shing, supra).

"Retinopathy" refers to inflammation of the retina and/or degenerative condition of the retina which may lead to occlusion of the retina and eventual blindness. "diabetic retinopathy" angiogenesis causes the capillaries in the retina to invade the vitreous resulting in bleeding 25 and blindness which is also seen in neonatal retinopathy (for a review see Folkman, 1985 supra; Folkman 1990 supra; Folkman and Shing, 1992 supra).

Example 1: flt-1, KDR and/or flk-1 ribozymes

20

By engineering ribozyme motifs applicant has designed 30 several ribozymes directed against flt-1, KDR and/or flk-1 encoded mRNA sequences. These ribozymes were synthesized with modifications that improve their nuclease resistance (Beigelman et al., 1995 J Biol. Chem. 270, 25702) and enhance their activity in cells. The ability of ribozymes 35 to cleave target sequences in vitro was evaluated essentially as described in Thompson et al., PCT Publication

27

No. WO 93/23057; Draper et al., PCT Publication No. WO 95/04818.

Example 2: Effect of ribozymes on the binding of VEGF to flt-1, KDR and/or flk-1 receptors

Several common human cell lines are available that express endogenous flt-1, KDR and/or flk-1. flt-1, KDR and/or flk-1 can be detected easily with monoclonal antibodies. Use of appropriate fluorescent reagents and fluorescence-activated cell-sorting (FACS) will permit direct quantitation of surface flt-1, KDR and/or flk-1 on a cell-by-cell basis. Active ribozymes are expected to directly reduce flt-1, KDR and/or flk-1 expression and thereby reduce VEGF binding to the cells. In this example, human umbelical cord microvascular endothelial cells were used.

Cell Preparation:

Plates are coated with 1.5% gelatin and allowed to stand for one hour. Cells (e.g., microvascular endothelial cells derived from human umbilical cord vein) are plated at 20,000 cells/well (24 well plate) in 200 ml growth media and incubated overnight (~ 1 doubling) to yield ~40,000 cells (75-80% confluent).

Ribozyme treatment:

Media is removed from cells and the cells are washed two times with 300 ml 1X PBS: Ca²⁺: Mg²⁺ mixture. A complex of 200-500 nM ribozyme and LipofectAMINE® (3:1 lipid: phosphate ratio) in 200 ml OptiMEM® (5% FBS) was added to the cells. The cells are incubated for 6 hr (equivalent to 2-3 VEGF-R turnovers).

30 125 I VEGF binding assay:

The assay is carried out on ice to inhibit internalization of VEGF during the experiment. The media containing the ribozyme is removed from the cells and the cells

are washed twice with with 300 ml 1X PBS: Ca²⁺: Mg²⁺ mixture containing 1% BSA. Appropriate ¹²⁵I VEGF solution (100,000 cpm/well, +/- 10 X cold 1X PBS, 1% BSA) was applied to the cells. The cells are incubated on ice for 1 h. ¹²⁵I VEGF-containing solution is removed and the cells are washed three times with with 300 ml 1X PBS: Ca²⁺: Mg²⁺ mixture containing 1% BSA. To each well 300 ml of 100 mM Tris-HCl, pH 8.0, 0.5% Triton X-100 was added and the the mixture was incubated for 2 min. The ¹²⁵I VEGF-binding was quantitated using standard scintillation counting techniques. Percent inhibition was calculated as follows:

Percent Inhibition =

cpm ¹²⁵I VEGF bound by the ribozyme-treated samples x 100 cpm ¹²⁵I VEGF bound by the Control sample

15 Example 3: Effect of hammerhead ribozymes targeted against flt-1 receptor on the binding of VEGF

Hammerhead ribozymes targeted to twenty sites within flt-1 RNA were synthesized as described above. Sequence of the ribozymes used are shown in Table II; the length of stem II region is 3 bp. The hammerhead ribozymes were chemically modified such that the ribozyme consists of ribose residues at five positions; U4 and U7 positions contain 2'-NH₂ modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions; four nucleotides at the 5' terminus contains phosphorothicate substitutions. Additionally, 3' end of the ribozyme contains a 3'-3' linked inverted abasic ribose.

Referring to Figure 7, the effect of hammerhead ribozymes targeted against flt-1 receptor on the binding of VEGF to flt-1 on the surface of human microvascular endothelial cells is shown. The majority of the ribozymes tested were able to inhibit the expression of flt-1 and thereby were able to inhibit the binding of VEGF.

In order to determine the specificity of ribozymes 35 targeted against flt-1 RNA, the effect of five anti-flt-1 ribozymes on the binding of VEGF, UPA (urokinase plasmino-

PCT/US96/17480 WO 97/15662

29

gen activator) and FGF (fibroblast growth factor) to their corresponding receptors were assayed. As shown in Figure 9, there was significant inhibition of VEGF binding to its receptors on cells treated with anti-flt-1 ribozymes. There was no specific inhibition of the binding of UPA and FGF to their corresponding receptors. These data strongly suggest that anti-flt-1 ribozymes specifically cleave flt-1 RNA and not RNAs encoding the receptors for UPA and FGF, resulting in the inhibition of flt-1 receptor expression on the surface of the cells. Thus the ribozymes are 10 responsible for the inhibition of VEGF binding but not the binding of UPA and FGF.

Example 4: Effect of hammerhead ribozymes targeted against KDR receptor on the binding of VEGF

15

35

Hammerhead ribozymes targeted to twenty one sites within KDR RNA were synthesized as described above. Sequence of the ribozymes used are shown in Table IV; the length of stem II region is 3 bp. The hammerhead ribozymes were chemically modified such that the ribozyme 20 consists of ribose residues at five positions; U4 and U7 positions contain 2'-NH, modifications, the remaining nucleotide positions contain 2'-O-methyl substitutions; four nucleotides at the 5' terminus contains phosphorothioate substitutions. Additionally, the 3' end of the 25 ribozyme contains a 3'-3' linked inverted abasic deoxyribose.

Referring to Figure 8, the effect of hammerhead ribozymes targeted against KDR receptor on the binding of VEGF to KDR on the surface of human microvascular endo-30 thelial cells is shown. A majority of the ribozymes tested were able to inhibit the expression of KDR and thereby were able to inhibit the binding of VEGF. As a control, the cells were treated with a ribozyme that is not targeted towards KDR RNA (irrel. RZ); there was no specific inhibition of VEGF binding. The results from this control experiment strongly suggest that the inhibi-

30

tion of VEGF binding observed with anti-KDR ribozymes is a ribozyme-mediated inhibition.

Example 5: Effect of ribozymes targeted against VEGF receptors on cell proliferation

5 Cell Preparation:

24-well plates are coated with 1.5% gelatin (porcine skin 300 bloom). After 1 hr, excess gelatin is washed off of the plate. Microvascular endothelial cells are plated at 5,000 cells/well (24 well plate) in 200 ml growth media. The cells are allowed to grow for ~ 18 hr (~ 1 doubling) to yield ~10,000 cells (25-30% confluent).

Ribozyme treatment:

Media is removed from the cells, and the cells are washed two times with 300 ml 1X PBS: Ca²⁺: Mg²⁺ mixture.

For anti-flt-1 HH ribozyme experiment (Figure 12) a complex of 500 nM ribozyme; 15 mM LFA (3:1 lipid:phosphate ratio) in 200 ml OptiMEM (5% FCS) media was added to the cells. Incubation of cells is carried out for 6 hr (equivalent to 2-3 VEGF receptor turnovers).

For anti-KDR HH ribozyme experiment (Figure 13) a complex of 200 nM ribozyme; 5.25 mM LFA (3:1 lipid: phosphate ratio) in 200 ml OptiMEM (5% FCS) media was added to the cells. Incubation of cells is carried out for 3 hr.

25 <u>Proliferation</u>:

After three or six hours, the media is removed from the cells and the cells are washed with 300 ml 1X PBS: Ca²⁺: Mg²⁺ mixture. Maintenance media (contains dialyzed 10% FBS) +/- VEGF or basic FGF at 10 ng/ml is added to the cells. The cells are incubated for 48 or 72 h. The cells are trypsinized and counted (Coulter counter). Trypan blue is added on one well of each treatment as control.

As shown in Figure 12B, VEGF and basic FGF can stimulate human microvascular endothelial cell proliferation. However, treatment of cells with 1358 HH or 4229 HH ribozymes, targeted against flt-1 mRNA, results in a significant decrease in the ability of VEGF to stimulate endothelial cell proliferation. These ribozymes do not inhibit the FGF-mediated stimulation of endothelial cell proliferation.

Human microvascular endothalial cells were also treated with hammerhead ribozymes targeted against sites 527, 730, 3702 or 3950 within the KDR mRNA. As shown in Figure 13, all four ribozymes caused significant inhibition of VEGF-mediated induction of cell proliferation. No significant inhibition of cell proliferation was observed when the cells were treated with a hammerhead ribozyme targeted to an irrelevant RNA. Additionally, none of the ribozymes inhibited FGF-mediated stimulation of cell proliferation.

These results strongly suggest that hammerhead 20 ribozymes targeted against either flt-1 or KDR mRNA can specifically inhibit VEGF-mediated induction of endothelial cell proliferation.

Example 6: Effect of antisense oligonucleotides targeted against VEGF receptors on cell proliferation (colorimetric assay)

Following are some of the reagents used in the proliferation assay:

<u>Cells:</u> Human aortic endothelial cells (HAEC) from Clonetics[®]. Cells at early passage are preferably used.

30 <u>Uptake Medium:</u> EBM (from Clonetics®);1% L-Glutamine;20 mM Hepes; No serum; No antibiotics.

Growth Medium: EGM (from Clonetics®); FBS to 20%;1% L-Glutamine; 20 mM Hepes.

Cell Plating: 96-well tissue culture plates are
35 coated with 0.2% gelatin (50 ml/well). The gelatin is
incubated in the wells at room temperature for 15-30

minutes. The gelatin is removed by aspiration and the wells are washed with PBS:Ca²⁺: Mg²⁺ mixture. PBS mixture is left in the wells until cells are ready to be added. HAEC cells were detached by trypsin treatment and resuspended at 1.25 x 10⁴/ml in growth medium. PBS is removed from plates and 200 ml of cells (i.e. 2.5 x 10³ cells/well) are added to each well. The cells are allowed to grow for 48 hours before the proliferation assay.

Assay: Growth medium is removed from the wells. 10 cells are washed twice with PBS:Ca2+: Mg2+ mixture without A formulation of lipid/antisense oligoantibiotics. nucleotide (antisense oligonucleotide is used here as a non-limiting example) complex is added to each well (100 ml/well) in uptake medium. The cells are incubated for 2-3 hours at 37°C in CO2 incubator. After uptake, 100 ml/well of growth medium is added (gives final FBS concentration of 10%). After approximately 72 hours, 40 ml MTS® stock solution (made as described by manufacturer) was added to each well and incubated at 37°C for 1-3 20 hours, depending on the color development. assay, 2 hours was sufficient). The intensity of color formation was determined on a plate reader at 490 nM.

Phosphorothioate-substituted antisense oligodeoxynucleotides were custom synthesized by The Midland 25 Certified Reagent Company®, Midland, Texas. Following non-limiting antisense oligodeoxynucleotides targeted against KDR RNA were used in the proliferation assay:

KDR 21 AS: 5'-GCA GCA CCT TGC TCT CCA TCC-3'
SCRAMBLED CONTROL: 5'-CTG CCA ACT TCC CAT GCC TGC-3'

As shown in Figure 10, proliferation of HAEC cells are specifically inhibited by increasing concentrations of the phosphorothicate anti-KDR-antisense oligodeoxynucleotide. The scrambled antisense oligonucleotide is not expected to bind the KDR RNA and therefore is not expected to inhibit KDR expression. As expected, there is no detectable inhibition of proliferation of HAEC cells

33

treated with a phosphorothicate antisense oligonucleotide with scrambled sequence.

Example 7: In vitro cleavage of flt-1 RNA by hammerhead ribozymes

Referring to Figure 11A, hammerhead ribozymes (HH) targeted against sites 1358 and 4229 within the flt-1 RNA were synthesized as described above.

RNA cleavage assay in vitro:

5

25

Substrate RNA was 5' end-labeled using [g-32P] ATP and 10 T4 polynucleotide kinase (US Biochemicals). Cleavage reactions were carried out under ribozyme "excess" conditions. Trace amount (≤ 1 nM) of 5' end-labeled substrate and 40 nM unlabeled ribozyme were denatured and renatured separately by heating to 90°C for 2 min and snap-cooling 15 on ice for 10-15 min. The ribozyme and substrate were incubated, separately, at 37°C for 10 min in a buffer containing 50 mM Tris-HCl and 10 mM MgCl2. The reaction was initiated by mixing the ribozyme and substrate solutions and incubating at 37°C. Aliquots of 5 ml are taken 20 at regular intervals of time and the reaction is quenched by mixing with equal volume of 2X formamide stop mix. The samples are resolved on 20 % denaturing polyacrylamide The results were quantified and percentage of target RNA cleaved is plotted as a function of time.

Referring to Figure 11B and 11C, hammerhead ribozymes targeted against sites 1358 and 4229 within the flt-1 RNA are capable of cleaving target RNA efficiently in vitro.

Example 8: In vitro cleavage of KDR RNA by hammerhead ribozymes

In this non-limiting example, hammerhead ribozymes targeted against sites 726, 527, 3702 and 3950 within KDR RNA were synthesized as described above. RNA cleavage reactions were carried out *in vitro* essentially as described under Example 7.

25

Referring to Figures 14 and 15, all four ribozymes were able to cleave their cognate target RNA efficiently in a sequence-specific manner.

Example 9: In vitro cleavage of RNA by hammerhead ribozymes targeted against cleavage sites that are homologous between KDR and flt-1 mRNA

Because flt-1 and KDR mRNAs are highly homologous in certain regions, some ribozyme target sites are also homologous (see Table X). In this case, a single ribozyme will target both flt-1 and KDR mRNAs. Hammerhead ribozyme (FLT/KDR-I) targeted against one of the homologous sites between flt-1 and KDR (flt-1 site 3388 and KDR site 3151) was synthesized as described above. Ribozymes with either a 3 bp stem II or a 4 bp stem II were synthesized.

15 RNA cleavage reactions were carried out in vitro essentially as described under Example 7.

Referring to Figure 16, FLT/KDR-I ribozyme with either a 3 or a 4 bp stem II was able to cleave its target RNA efficiently in vitro.

20 Example 10: Effect of multiple ribozymes targeted against both flt-1 and KDR RNA on cell proliferation

Since both flt-1 and KDR receptors of VEGF are involved in angiogenesis, the inhibition of the expression of both of these genes may be an effective approach to inhibit angiogenesis.

Human microvascular endothalial cells were treated with hammerhead ribozymes targeted against sites flt-1 4229 alone, KDR 527 alone, KDR 726 alone, KDR 3950 alone, flt-1 4229 + KDR 527, flt-1 4229 + KDR 726 or flt-1 4229 + KDR 3950. As shown in Figure 17, all the combinations of active ribozymes (A) caused significant inhibition of VEGF-mediated induction of cell proliferation. No significant inhibition of cell proliferation was observed when the cells were treated with a catalytically inactive 35 (I) hammerhead ribozymes. Additionally, cells treated

with ribozymes targeted against both flt-1 and KDR RNAsflt-1 4229 + KDR 527; flt-1 4229 + KDR 726; flt-1 4229 +
KDR 3950, were able to cause a greater inhibition of
VEGF-mediated induction of cell proliferation when
compared with individual ribozymes targeted against either
flt-1 or KDR RNA (see flt-1 4229 alone; KDR 527 alone; KDR
726 alone; KDR 3950 alone). This strongly suggests that
treatment of cells with multiple ribozymes may be a more
effective means of inhibition of gene expression.

10 Animal Models

There are several animal models in which the anti-angiogenesis effect of nucleic acids of the present invention, such as ribozymes, directed against VEGF-R mRNAs can be tested. Typically a corneal model has been 15 used to study angiogenesis in rat and rabbit since recruitment of vessels can easily be followed in this normally avascular tissue (Pandey et al., 1995 Science 268: 567-569). In these models, a small Teflon or Hydron disk pretreated with an angiogenesis factor (e.g. bFGF or 20 VEGF) is inserted into a pocket surgically created in the cornea. Angiogenesis is monitored 3 to 5 days later. Ribozymes directed against VEGF-R mRNAs would be delivered in the disk as well, or dropwise to the eye over the time course of the experiment. In another eye model, hypoxia has been shown to cause both increased expression of VEGF and neovascularization in the retina (Pierce et al., 1995 Proc. Natl. Acad. Sci. USA. 92: 905-909; Shweiki et al., 1992 J. Clin. Invest. 91: 2235-2243).

In human glioblastomas, it has been shown that VEGF is at least partially responsible for tumor angiogenesis (Plate et al., 1992 Nature 359, 845). Animal models have been developed in which glioblastoma cells are implanted subcutaneously into nude mice and the progress of tumor growth and angiogenesism is studied (Kim et al., 1993 supra; Millauer et al., 1994 supra).

Another animal model that addresses neovascularization involves Matrigel, an extract of basement membrane that becomes a solid gel when injected subcutaneously (Passaniti et al., 1992 Lab. Invest. 67: 519-528). When the Matrigel is supplemented with angiogenesis factors such as VEGF, vessels grow into the Matrigel over a period of 3 to 5 days and angiogenesis can be assessed. Again, ribozymes directed against VEGF-R mRNAs would be delivered in the Matrigel.

Several animal models exist for screening of anti-10 angiogenic agents. These include corneal vessel formation following corneal injury (Burger et al., 1985 Cornea 4: 35-41; Lepri, et al., 1994 J. Ocular Pharmacol. 10: 273-280; Ormerod et al., 1990 Am. J. Pathol. 137: 1243-1252) 15 or intracorneal growth factor implant (Grant et al., 1993 Diabetologia 36: 282-291; Pandey et al. 1995 supra; Zieche et al., 1992 Lab. Invest. 67: 711-715), vessel growth into Matrigel matrix containing growth factors (Passaniti et al., 1992 supra), female reproductive organ neovasculari-20 zation following hormonal manipulation (Shweiki et al., 1993 Clin. Invest. 91: 2235-2243), several models involving inhibition of tumor growth in highly vascularized solid tumors (O'Reilly et al., 1994 Cell 79: 315-328; Senger et al., 1993 Cancer and Metas. Rev. 12: 303-324; Takahasi et al., 1994 Cancer Res. 54: 4233-4237; Kim et transient 1993 supra), and hypoxia-induced neovascularization in the mouse retina (Pierce et al., 1995 Proc. Natl. Acad. Sci. USA. 92: 905-909).

The cornea model, described in Pandey et al. supra,

is the most common and well characterized anti-angiogenic agent efficacy screening model. This model involves an avascular tissue into which vessels are recruited by a stimulating agent (growth factor, thermal or alkalai burn, endotoxin). The corneal model would utilize the intrastromal corneal implantation of a Teflon pellet soaked in a VEGF-Hydron solution to recruit blood vessels toward the pellet which can be quantitated using standard microscopic

and image analysis techniques. To evaluate their antiangiogenic efficacy, ribozymes are applied topically to
the eye or bound within Hydron on the Teflon pellet
itself. This avascular cornea as well as the Matrigel
(see below) provide for low background assays. While the
corneal model has been performed extensively in the
rabbit, studies in the rat have also been conducted.

The mouse model (Passaniti et al., supra) is a non-tissue model which utilizes Matrigel, an extract of 10 basement membrane (Kleinman et al., 1986) or Millipore® filter disk, which can be impregnated with growth factors and anti-angiogenic agents in a liquid form prior to Upon subcutaneous administration at body injection. temperature, the Matrigel or Millipore® filter disk forms VEGF embedded in the Matrigel or 15 a solid implant. Millipore® filter disk would be used to recruit vessels within the matrix of the Matrigel or Millipore® filter disk which can be processed histologically for endothelial cell specific vWF (factor VIII antigen) immunohisto-20 chemistry, Trichrome-Masson stain, or hemoglobin content. Like the cornea, the Matrigel or Millipore® filter disk are avascular; however, it is not tissue. In the Matrigel or Millipore® filter disk model, ribozymes are administered within the matrix of the Matrigel or Millipore® 25 filter disk to test their anti-angiogenic efficacy. delivery issues in this model, as with delivery of ribozymes by Hydron-coated Teflon pellets in the rat cornea model, may be less problematic due to the homogeneous presence of the ribozyme within the respective matrix.

These models offer a distinct advantage over several other angiogenic models listed previously. The ability to use VEGF as a pro-angiogenic stimulus in both models is highly desirable since ribozymes will target only VEGFr mRNA. In other words, the involvement of other non-specific types of stimuli in the cornea and Matrigel models is not advantageous from the standpoint of understanding the pharmacologic mechanism by which the

anti-VEGFr mRNA ribozymes produce their effects. In addition, the models will allow for testing the specificity of the anti-VEGFr mRNA ribozymes by using either a- or bFGF as a pro-angiogenic factor. Vessel recruitment using FGF 5 should not be affected in either model by anti-VEGFr mRNA ribozymes. Other models of angiogenesis including vessel formation in the female reproductive system using hormonal manipulation (Shweiki et al., 1993 supra); a variety of vascular solid tumor models which involve indirect cor-10 relations with angiogenesis (O'Reilly et al., 1994 supra; Senger et al., 1993 supra; Takahasi et al., 1994 supra; Kim et al., 1993 supra); and retinal neovascularization following transient hypoxia (Pierce et al., 1995 supra) were not selected for efficacy screening due to their 15 non-specific nature, although there is a correlation between VEGF and angiogenesis in these models.

Other model systems to study tumor angiogenesis is reviewed by Folkman, 1985 Adv. Cancer. Res.. 43, 175.

flt-1, KDR and/or flk-1 protein levels can be measured clinically or experimentally by FACS analysis. flt-1, KDR and/or flk-1 encoded mRNA levels will be assessed by Northern analysis, RNase-protection, primer extension analysis and/or quantitative RT-PCR. Ribozymes that block flt-1, KDR and/or flk-1 protein encoding mRNAs and therefore result in decreased levels of flt-1, KDR and/or flk-1 activity by more than 20% in vitro will be identified.

Ribozymes and/or genes encoding them are delivered by either free delivery, liposome delivery, cationic lipid delivery, adeno-associated virus vector delivery, adenovirus vector delivery, retrovirus vector delivery or plasmid vector delivery in these animal model experiments (see above).

Patients can be treated by locally administering nucleic acids targeted against VEGF-R by direct injection. Routes of administration may include, but are not limited to, intravascular, intramuscular, subcutaneous, intra-

PCT/US96/17480 WO 97/15662

39

articular, aerosol inhalation, oral (tablet, capsule or pill form), topical, systemic, ocular, intraperitoneal and/or intrathecal delivery.

Example 11: Ribozyme-mediated inhibition of angiogenesis 5 in vivo

The purpose ot this study was to assess the antiangiogenic activity of hammerhead ribozymes targeted against flt-1 4229 site in the rat cornea model of VEGF induced angiogenesis (see above). These ribozymes have 10 either active or inactive catalytic core and either bind and cleave or just bind to VEGF-R mRNA of the flt-1 subtype. The active ribozymes, that are able to bind and cleave the target RNA, have been shown to inhibit (125I-labeled) VEGF binding in cultured endothelial cells 15 and produce a dose-dependent decrease in VEGF induced endothelial cell proliferation in these cells Examples 3-5 above). The catalytically inactive forms of these ribozymes, wherein the ribozymes can only bind to the RNA but cannot catalyze RNA cleavage, fail to show these characteristics. The ribozymes and VEGF were co-delivered using the filter disk method: Nitrocellulose filter disks (Millipore®) of 0.057 diameter were immersed in appropriate solutions and were surgically implanted in rat cornea as described by Pandey et al., supra. 25 delivery method has been shown to deliver rhodaminelabeled free ribozyme to scleral cells and, likelihood cells of the pericorneal vascular plexus. Since the active ribozymes show cell culture efficacy and can be delivered to the target site using the disk method, it is essential that these ribozymes be assessed for in vivo anti-angiogenic activity.

The stimulus for angiogenesis in this study was the treatment of the filter disk with 30 mM VEGF which is implanted within the cornea's stroma. This dose yields 35 reproducible neovascularization stemming from the pericorneal vascular plexus growing toward the disk in a

dose-response study 5 days following implant. Filter disks treated only with the vehicle for VEGF show no angiogenic response. The ribozymes was co-adminstered with VEGF on a disk in two different ribozyme concentrations. One concern with the simultaneous administration is that the ribozymes will not be able to inhibit angiogenesis since VEGF receptors can be stimulated. However, we have observed that in low VEGF doses, the neovascular response reverts to normal suggesting that the VEGF stimulus is essential for maintaining the angiogenic response. Blocking the production of VEGF receptors using simultaneous administration of anti-VEGF-R mRNA ribozymes could attenuate the normal neovascularization induced by the filter disk treated with VEGF.

15 Materials and Methods:

- Stock hammerhead ribozyme solutions:
 - a. flt-1 4229 (786 μ M) Active
 - b. flt-1 4229 (736 μ M) Inactive

2. Experimental solutions/groups:

20	Group 1	Solution 1	Control VEGF solution: 30 μM in
			82mM Tris base
	Group 2	Solution 2	flt-1 4229 (1 μ g/ μ L) in 30 μ M
			VEGF/82 mM Tris base
	Group 3	Solution 3	flt-1 4229 (10 $\mu g/\mu L$) in 30 μM
25			VEGF/82 mM Tris base
	Group 4	Solution 4	No VEGF, flt-1 4229 (10 μ g/ μ L)
			in 82 mM Tris base
	Group 5	Solution 5	No VEGF, No ribozyme in 82 mM
			Tris base

30 10 eyes per group, 5 animals (Since they have similar molecular weights, the molar concentrations should be essentially similar).

Each solution (VEGF and RIBOZYMES) were prepared as a 2X solution for 1:1 mixing for final concentrations

41

above, with the exception of solution 1 in which VEGF was 2X and diluted with ribozyme diluent (sterile water).

3. VEGF Solutions

The 2X VEGF solution (60 μ M) was prepared from a stock of 0.82 μ g/ μ L in 50 mM Tris base. 200 μ L of VEGF stock was concentrated by speed vac to a final volume of 60.8 μ L, for a final concentration of 2.7 μ g/ μ L or 60 μ M. Six 10 μ L aliquots was prepared for daily mixing. 2X solutions for VEGF and Ribozyme was stored at 4°C until the day of the surgery. Solutions were mixed for each day of surgery. Original 2X solutions was prepared on the day before the first day of the surgery.

4. Surgical Solutions:

Anesthesia:

20

stock ketamine hydrochloride 100 mg/mL stock xylazine hydrochloride 20 mg/mL stock acepromazine 10 mg/mL

Final anesthesia solution: 50 mg/mL ketamine, 10 mg/mL xylazine, and 0.5 mg/mL acepromazine
5% povidone iodine for opthalmic surgical wash
2% lidocaine (sterile) for opthalmic administration (2 drops per eye)
sterile 0.9% NaCl for opthalmic irrigation

5. <u>Surgical Methods</u>:

Standard surgical procedure as described in Pandey et al., supra. Filter disks were incubated in 1 μ L of each solution for approximately 30 minutes prior to implantation.

5. Experimental Protocol:

The animal cornea were treated with the treatment groups as described above. Animals were allowed to recover for 5 days after treatment with daily observation (scoring 0 - 3). On the fifth day animals were euthanized and

PCT/US96/17480 WO 97/15662

digital images of each eye was obtained for quantitaion using Image Pro Plus. Quantitated neovascular surface area were analyzed by ANOVA followed by two post-hoc tests including Dunnets and Tukey-Kramer tests for significance 5 at the 95% confidence level. Dunnets provide information on the significance between the differences within the means of treatments vs. controls while Tukey-Kramer provide information on the significance of differences within the means of each group.

Results are graphically represented in Figure 18. 10 shown in the figure, flt-1 4229 active hammerhead ribozyme at both concentrations was effective at inhibiting angiogenesis while the inactive ribozyme did not show any significant reduction in angiogenesis. A statistically 15 signifiant reduction in neovascular surface area was observed only with active ribozymes. This result clearly shows that the ribozymes are capable of significantly inhibiting angiogenesis in vivo. Specifically, mechanism of inhibition appears to be by the binding and 20 cleavage of target RNA by ribozymes.

Diagnostic uses

35

Ribozymes of this invention may be used as diagnostic tools to examine genetic drift and mutations within diseased cells or to detect the presence of flt-1, KDR and/or flk-1 RNA in a cell. The close relationship 25 between ribozyme activity and the structure of the target RNA allows the detection of mutations in any region of the molecule which alters the base-pairing and dimensional structure of the target RNA. By using multiple ribozymes described in this invention, one may map nucleotide changes which are important RNA structure and function in vitro, as well as in cells and tissues. Cleavage of target RNAs with ribozymes may be used to inhibit gene expression and define the role (essentially) of specified gene products in the progression of disease. In this manner, other genetic targets

may be defined as important mediators of the disease. These experiments will lead to better treatment of the disease progression by affording the possibility of combinational therapies (e.g., multiple ribozymes targeted to different genes, ribozymes coupled with known small molecule inhibitors, or intermittent treatment combinations of ribozymes and/or other chemical biological molecules). Other in vitro uses of ribozymes of this invention are well known in the art, and include 10 detection of the presence of mRNAs associated with flt-1, KDR and/or flk-1 related condition. Such RNA is detected by determining the presence of a cleavage product after treatment with a ribozyme using standard methodology.

In a specific example, ribozymes which can cleave only wild-type or mutant forms of the target RNA are used for the assay. The first ribozyme is used to identify wild-type RNA present in the sample and the second ribozyme will be used to identify mutant RNA in the sample. As reaction controls, synthetic substrates of both wildtype and mutant RNA will be cleaved by both ribozymes to 20 demonstrate the relative ribozyme efficiencies in the reactions and the absence of cleavage of the "nontargeted" RNA species. The cleavage products from the synthetic substrates will also serve to generate size markers for the analysis of wild-type and mutant RNAs in the sample population. Thus each analysis will require two ribozymes, two substrates and one unknown sample which will be combined into six reactions. The presence of cleavage products will be determined using an RNAse protection assay so that full-length and cleavage fragments of each RNA can be analyzed in one lane of a polyacrylamide gel. It is not absolutely required to quantify the results to gain insight into the expression of mutant RNAs and putative risk of the desired phenotypic changes in target cells. The expression of mRNA whose protein product is implicated in the development of the phenotype (i.e., flt-1, KDR and/or flk-1) is adequate to establish

44

risk. If probes of comparable specific activity are used for both transcripts, then a qualitative comparison of RNA levels will be adequate and will decrease the cost of the initial diagnosis. Higher mutant form to wild-type ratios will be correlated with higher risk whether RNA levels are compared qualitatively or quantitatively.

Other embodiments are within the following claims.

45

Table I

:

Characteristics of Ribozymes

Group I Introns

Size: ~200 to >1000 nucleotides

5 Requires a U in the target sequence immediately 5' of the cleavage site.

Binds 4-6 nucleotides at 5' side of cleavage site.

Over 75 known members of this class. Found in *Tetrahymena* thermophila rRNA, fungal mitochondria, chloroplasts, phage

10 T4, blue-green algae, and others.

RNAseP RNA (M1 RNA)

Size: ~290 to 400 nucleotides

RNA portion of a ribonucleoprotein enzyme. Cleaves tRNA precursors to form mature tRNA.

15 Roughly 10 known members of this group all are bacterial in origin.

Hammerhead Ribozyme

Size: ~13 to 40 nucleotides.

Requires the target sequence UH immediately 5' of the 20 cleavage site.

Binds a variable number of nucleotides on both sides of the cleavage site.

14 known members of this class. Found in a number of plant pathogens (virusoids) that use RNA as the infectious 25 agent (Figure 1 and 2)

Hairpin Ribozyme

Size: ~50 nucleotides.

Requires the target sequence GUC immediately 3' of the cleavage site.

30 Binds 4-6 nucleotides at 5' side of the cleavage site and a variable number to the 3' side of the cleavage site.

Only 3 known member of this class. Found in three plant pathogen (satellite RNAs of the tobacco ringspot virus,

PCT/US96/17480

arabis mosaic virus and chicory yellow mottle virus) which uses RNA as the infectious agent (Figure 3).

Hepatitis Delta Virus (HDV) Ribozyme

Size: 50-60 nucleotides (at present)

5 Sequence requirements not fully determined.

Binding sites and structural requirements not fully determined, although no sequences 5' of cleavage site are required.

Only 1 known member of this class. Found in human HDV 10 (Figure 4).

Neurospora VS RNA Ribozyme

Size: ~144 nucleotides (at present)

Cleavage of target RNAs recently demonstrated.

Sequence requirements not fully determined.

15 Binding sites and structural requirements not fully determined. Only 1 known member of this class. Found in Neurospora VS RNA (Figure 5).

Table II: Human flt1 VEGF Receptor-Hammerhead Ribozyme and Substrate Sequence

20	nt. Posi- tion		HH Ri	bo	zyme		Sub	strate
	10	GCCGAGAG	CUGAUGA	x	GAA	AGUGUCCG	CGGACACU	CUCUCGGC
	13	GGAGCCGA	CUGAUGA	x	GAA	AGGAGUGU	ACACUCCUC	ucggcucc
25	15	GAGGAGCC	CUGAUGA	x	GAA	AGAGGAGU	ACUCCUCUC	GGCUCCUC
	20	CCGGGGAG	CUGAUGA	x	GAA	AGCCGAGA	UCUCGGCU	CUCCCCGG
	23	CUGCCGGG	CUGAUGA	X	GAA	AGGAGCCG	CGGCUCCUC	CCCGGCAG
	43	CCCGCUCC	CUGAUGA	X	GAA	AGCCGCCG	CGGCGGCU	GGAGCGGG
	54	GAGCCCCG	CUGAUGA	X	GAA	AGCCCGCU	AGCGGGCU	CGGGGCUC
30	62	CUGCACCC	CUGAUGA	X	GAA	AGCCCCGG	CCGGGGCU	GGGUGCAG
	97	ccccggu	CUGAUGA	X	GAA	AUCCUCGC	GCGAGGAUT	ACCCGGGG
	98	UCCCCGGG	CUGAUGA	X	GAA	AAUCCUCG	CGAGGAUU	CCCGGGGA

	113	CAGGAGAC	CUGAUGA	X	GAA	ACCACUUC	GAAGUGGUU	GUCUCCUG
	116	AGCCAGGA	CUGAUGA	X	GAA	ACAACCAC	GUGGUUGUC	UCCUGGCU
	118	CCAGCCAG	CUGAUGA	X	GAA	AGACAACC	GGUUGUCUC	CUGGCUGG
	145	CGCGCCCU	CUGAUGA	X	GAA	AGCGCCCG	CGGGCGCUC	AGGGCGCG
5	185	GGCCGCCA	CUGAUGA	X	GAA	AGUCCGUC	GACGGACUC	UGGCGGCC
	198	CGGCCAAC	CUGAUGA	X	GAA	ACCCGGCC	GGCCGGGUC	GUUGGCCG
	201	CCCCGGCC	CUGAUGA	X	GAA	ACGACCCG	CGGGUCGUU	GGCCGGGG
	240	GUGAGCGC	CUGAUGA	X	GAA	ACGCGGCC	GGCCGCGUC	GCGCUCAC
	246	ACCAUGGU	CUGAUGA	X	GAA	AGCGCGAC	GUCGCGCUC	ACCAUGGU
10	255	CAGUAGCU	CUGAUGA	X	GAA	ACCAUGGU	ACCAUGGUC	AGCUACUG
	260	UGUCCCAG	CUGAUGA	X	GAA	AGCUGACC	GGUCAGCUA	CUGGGACA
	276	CACAGCAG	CUGAUGA	X	GAA	ACCCCGGU	ACCGGGGUC	CUGCUGUG
	294	AGACAGCU	CUGAUGA	X	GAA	AGCAGCGC	GCGCUGCUC	AGCUGUCU
	301	GAGAAGCA	CUGAUGA	X	GAA	ACAGCUGA	UCAGCUGUC	UGCUUCUC
15	306	CCUGUGAG	CUGAUGA	X	GAA	AGCAGACA	UGUCUGCUU	CUCACAGG
	307	UCCUGUGA	CUGAUGA	X	GAA	AAGCAGAC	GUCUGCUUC	UCACAGGA
	309	GAUCCUGU	CUGAUGA	X	GAA	AGAAGCAG	CUGCUUCUC	ACAGGAUC
	317	CUGAACUA	CUGAUGA	X	GAA	AUCCUGUG	CACAGGAUC	UAGUUCAG
	319	ACCUGAAC	CUGAUGA	X	GAA	AGAUCCUG	CAGGAUCUA	GUUCAGGU
20	322	UGAACCUG	CUGAUGA	X	GAA	ACUAGAUC	GAUCUAGUU	CAGGUUCA
	323	UUGAACCU	CUGAUGA	X	GAA	AACUAGAU	AUCUAGUUC	AGGUUCAA
	328	UAAUUUUG	CUGAUGA	X	GAA	ACCUGAAC	GUUCAGGUU	CAAAAUUA
	329	UUUAAUUU	CUGAUGA	X	GAA	AACCUGAA	UUCAGGUUC	AAUUAA
	335	GAUCUUUU	CUGAUGA	X	GAA	AUUUUGAA	UUCAAAAUU	AAAAGAUC
25	336	GGAUCUUU	CUGAUGA	X	GAA	AAUUUUGA	UCAAAAUUA	AAAGAUCC
	343	CAGUUCAG	CUGAUGA	X	GAA	AUCUUUUA	UAAAAGAUC	CUGAACUG
	355	GCCUUUUA	CUGAUGA	X	GAA	ACUCAGUU	AACUGAGUU	UAAAAGGC
	356	UGCCUUUU	CUGAUGA	X	GAA	AACUCAGU	ACUGAGUUU	AAAAGGCA
	357	GUGCCUUU	CUGAUGA	X	GAA	AAACUCAG	CUGAGUUUA	AAAGGCAC
30	375	GCUUGCAU	CUGAUGA	X	GAA	AUGUGCUG	CAGCACAUC	AUGCAAGC
	400	GCAUUGGA	CUGAUGA	X	GAA	AUGCAGUG	CACUGCAUC	UCCAAUGC
	402	CUGCAUUG	CUGAUGA	X	GAA	AGAUGCAG	CUGCAUCUC	CAAUGCAG
	427	AGACCAUU	CUGAUGA	X	GAA	AUGGGCUG	CAGCCCAUA	AAUGGUCU

	434	CAGGCAAA	CUGAUGA	X	GAA	ACCAUUUA	UAAAUGGUC	UUUGCCUG
	436	UUCAGGCA	CUGAUGA	X	GAA	AGACCAUU	AAUGGUCUU	UGCCUGAA
	437	UUUCAGGC	CUGAUGA	X	GAA	AAGACCAU	AUGGUCUUU	GCCUGAAA
	454	GCUUUCCU	CUGAUGA	X	GAA	ACUCACCA	UGGUGAGUA	AGGAAAGC
5	477	GAUUUAGU	CUGAUGA	X	GAA	AUGCUCAG	CUGAGCAUA	ACUAAAUC
	481	GGCAGAUU	CUGAUGA	X	GAA	AGUUAUGC	GCAUAACUA	AAUCUGCC
	485	CACAGGCA	CUGAUGA	X	GAA	AUUUAGUU	AACUAAAUC	UGCCUGUG
	512	UACUGCAG	CUGAUGA	X	GAA	AUUGUUUG	CAAACAAUU	CUGCAGUA
	51 3	GUACUGCA	CUGAUGA	X	GAA	AAUUGUUU	AAACAAUUC	UGCAGUAC
10	520	GGUUAAAG	CUGAUGA	X	GAA	ACUGCAGA	UCUGCAGUA	CUUUAACC
	52 3	CAAGGUUA	CUGAUGA	X	GAA	AGUACUGC	GCAGUACUU	UAACCUUG
	524	UCAAGGUU	CUGAUGA	X	GAA	AAGUACUG	CAGUACUUU	AACCUUGA
	52 5	UUCAAGGU	CUGAUGA	X	GAA	AAAGUACU	AGUACUUUA	ACCUUGAA
	530	CUGUGUUC	CUGAUGA	X	GAA	AGGUUAAA	UUUAACCUU	GAACACAG
15	541	GUUUGCUU	CUGAUGA	X	GAA	AGCUGUGU	ACACAGCUC	AAGCAAAC
	560	AGCUGUAG	CUGAUGA	X	GAA	AGCCAGUG	CACUGGCUU	CUACAGCU
	561	CAGCUGUA	CUGAUGA	X	GAA	AAGCCAGU	ACUGGCUUC	UACAGCUG
	563	UGCAGCUG	CUGAUGA	X	GAA	AGAAGCCA	UGGCUUCUA	CAGCUGCA
	575	CAGCUAGA	CUGAUGA	X	GAA	AUUUGCAG	CUGCAAAUA	UCUAGCUG
20	5 7 7	UACAGCUA	CUGAUGA	X	GAA	AUAUUUGC	GCAAAUAUC	UAGCUGUA
	579	GGUACAGC	CUGAUGA	X	GAA	AGAUAUUU	AAAUAUCUA	GCUGUACO
	585	GAAGUAGG	CUGAUGA	X	GAA	ACAGCUAG	CUAGCUGUA	CCUACUUC
	58 9	CUUUGAAG	CUGAUGA	X	GAA	AGGUACAG	CUGUACCUA	CUUCAAAG
	592	CUUCUUUG	CUGAUGA	X	GAA	AGUAGGUA	UACCUACUU	CAAAGAAG
25	593	ບບບບບບບບ	CUGAUGA	X	GAA	AAGUAGGU	ACCUACUUC	AAAGAAGA
	614	AGAUUGCA	CUGAUGA	X	GAA	AUUCUGUU	AACAGAAUC	UGCAAUCU
	621	AAUAUAUA	CUGAUGA	X	GAA	AUUGCAGA	UCUGCAAUC	UAUAUAUU
	623	AUAUAAU	CUGAUGA	X	GAA	AGAUUGCA	UGCAAUCUA	UAUAUUUA
	625	AUAAAUA	CUGAUGA	X	GAA	AUAGAUUG	CAAUCUAUA	UAUUUAU
30	627	CUAAUAAA	CUGAUGA	X	GAA	AUAUAGAU	AUCUAUAUA	CAUUAUUU
	62 9	CACUAAUA	CUGAUGA	X	GAA	AUAUAUAG	CUAUAUAUU	UAUUAGUO
	630	UCACUAAU	CUGAUGA	X	GAA	AUAUAUA	UUUAUAUAU	AUUAGUGA
	631	AUCACUAA	CUGAUGA	X	GAA	UAUAUAAA	AUUUAUUUA	UUAGUGAI

49

:

	633	GUAUCACU	CUGAUGA	X	GAA	AUAAAUAU	AUAUUUAUU	AGUGAUAC
	634	UGUAUCAC	CUGAUGA	X	GAA	AAUAAAUA	AUUAUUAU	GUGAUACA
	640	UCUACCUG	CUGAUGA	X	GAA	AUCACUAA	UUAGUGAUA	CAGGUAGA
	646	GAAAGGUC	CUGAUGA	X	GAA	ACCUGUAU	AUACAGGUA	GACCUUUC
5	652	CUCUACGA	CUGAUGA	X	GAA	AGGUCUAC	GUAGACCUU	UCGUAGAG
	653	UCUCUACG	CUGAUGA	X	GAA	AAGGUCUA	UAGACCUUU	CGUAGAGA
	654	AUCUCUAC	CUGAUGA	X	GAA	AAAGGUCU	AGACCUUUC	GUAGAGAU
	657	UACAUCUC	CUGAUGA	X	GAA	ACGAAAGG	CCUUUCGUA	GAGAUGUA
	665	UUUCACUG	CUGAUGA	X	GAA	ACAUCUCU	AGAGAUGUA	CAGUGAAA
10	67 5	AUUUCGGG	CUGAUGA	X	GAA	AUUUCACU	AGUGAAAUC	CCCGAAAU
	684	AUGUGUAU	CUGAUGA	X	GAA	AUUUCGGG	CCCGAAAUU	AUACACAU
	685	CAUGUGUA	CUGAUGA	X	GAA	AAUUUCGG	CCGAAAUUA	UACACAUG
	687	GUCAUGUG	CUGAUGA	X	GAA	AUAAUUUC	GAAAUUAUA	CACAUGAC
	711	GGAAUGAC	CUGAUGA	X	GAA	AGCUCCCU	AGGGAGCUC	GUCAUUCC
15	714	CAGGGAAU	CUGAUGA	X	GAA	ACGAGCUC	GAGCUCGUC	AUUCCCUG
	717	CGGCAGGG	CUGAUGA	X	GAA	AUGACGAG	CUCGUCAUU	CCCUGCCG
	718	CCGGCAGG	CUGAUGA	X	GAA	AAUGACGA	UCGUCAUUC	CCUGCCGG
	729	GGUGACGU	CUGAUGA	x	GAA	ACCCGGCA	UGCCGGGUU	ACGUCACO
	730	AGGUGACG	CUGAUGA	X	GAA	AACCCGGC	GCCGGGUUA	CGUCACCU
20	734	UGUUAGGU	CUGAUGA	X	GAA	ACGUAACC	GGUUACGUC	ACCUAACA
	739	AGUGAUGU	CUGAUGA	X	GAA	AGGUGACG	CGUCACCUA	ACAUCACU
	744	GUAACAGU	CUGAUGA	X	GAA	AUGUUAGG	CCUAACAUC	ACUGUUAC
	7 50	UUUAAAGU	CUGAUGA	X	GAA	ACAGUGAU	AUCACUGUU	ACUUUAAA
	751	UUUUAAAG	CUGAUGA	X	GAA	AACAGUGA	UCACUGUUA	CUUUAAAA
25	754	CUUUUUUA	CUGAUGA	X	GAA	AGUAACAG	CUGUUACUU	UAAAAAAG
	755	ACUUUUUU	CUGAUGA	X	GAA	AAGUAACA	UGUUACUUU	AAAAAAGU
	756	AACUUUUU	CUGAUGA	X	GAA	AAAGUAAC	GUUACUUUA	AAAAAGUU
	764	CAAGUGGA	CUGAUGA	X	GAA	ACUUUUUU	AAAAAAGUU	UCCACUUG
	765	UCAAGUGG	CUGAUGA	X	GAA	AACUUUUU	AAAAAGUUU	CCACUUGA
30	766	GUCAAGUG	CUGAUGA	X	GAA	AAACUUUU	AAAAGUUUC	CACUUGAC
	771	AAAGUGUC	CUGAUGA	X	GAA	AGUGGAAA	UUUCCACUU	GACACUUU
	778	AGGGAUCA	CUGAUGA	X	GAA	AGUGUCAA	UUGACACUU	UGAUCCCU
	779	CAGGGAUC	CUGAUGA	х	GAA	AAGUGUCA	UGACACUUU	GAUCCCUG

PCT/US96/17480

GAGGCCAUA CUCUUGUC

WO 97/15662

50

CCAUCAGG CUGAUGA X GAA AUCAAAGU ACUUUGAUC CCUGAUGG 783 UCCCAGAU CUGAUGA X GAA AUGCGUUU AAACGCAUA AUCUGGGA 801 CUGUCCCA CUGAUGA X GAA AUUAUGCG CGCAUAAUC UGGGACAG 804 GCCCUUUC CUGAUGA X GAA ACUGUCCC GGGACAGUA GAAAGGGC 814 AUAUGAUG CUGAUGA X GAA AGCCCUUU AAAGGGCUU CAUCAUAU 824 GAUAUGAU CUGAUGA X GAA AAGCCCUU AAGGGCUUC AUCAUAUC 825 UUUGAUAU CUGAUGA X GAA AUGAAGCC GGCUUCAUC AUAUCAAA 828 GCAUUUGA CUGAUGA X GAA AUGAUGAA UUCAUCAUA UCAAAUGC 831 UUGCAUUU CUGAUGA X GAA AUAUGAUG CAUCAUAUC AAAUGCAA ·833 UGCAACGUA CAAAGAAA UUUCUUUG CUGAUGA X GAA ACGUUGCA 10 845 AAAGAAAUA GGGCUUCU AGAAGCCC CUGAUGA X GAA AUUUCUUU 855 CAGGUCAG CUGAUGA X GAA AGCCCUAU AUAGGGCUU CUGACCUG 861 ACAGGUCA CUGAUGA X GAA AAGCCCUA UAGGGCUUC UGACCUGU 862 UGCCCAUU CUGAUGA X GAA ACUGUUGC GCAACAGUC AAUGGGCA 882 AUGGGCAUU UGUAUAAG CUUAUACA CUGAUGA X GAA AUGCCCAU 15 892 UGGGCAUUU GUAUAAGA UCUUAUAC CUGAUGA X GAA AAUGCCCA 893 UUGUCUUA CUGAUGA X GAA ACAAAUGC GCAUUUGUA UAAGACAA 896 GUUUGUCU CUGAUGA X GAA AUACAAAU AUUUGUAUA AGACAAAC 898 GUGUGAGA CUGAUGA X GAA AGUUUGUC GACAAACUA UCUCACAC 908 AUGUGUGA CUGAUGA X GAA AUAGUUUG CAAACUAUC UCACACAU 20 910 CGAUGUGU CUGAUGA X GAA AGAUAGUU AACUAUCUC ACACAUCG 912 UCACACAUC GACAAACC GGUIJIGUC CUGAUGA X GAA AUGUGUGA 919 UAUGAUUG CUGAUGA X GAA AUUGGUUU AAACCAAUA CAAUCAUA 931 ACAUCUAU CUGAUGA X GAA AUUGUAUU AAUACAAUC AUAGAUGU 936 ACAAUCAUA GAUGUCCA UGGACAUC CUGAUGA X GAA AUGAUUGU 25 939 AUAGAUGUC CAAAUAAG CUUAUUUG CUGAUGA X GAA ACAUCUAU 945 GGUGUGCU CUGAUGA X GAA AUUUGGAC GUCCAAAUA AGCACACC 951 AGUAAUUU CUGAUGA X GAA ACUGGGCG CGCCCAGUC AAAUUACU 969 CUCUAAGU CUGAUGA X GAA AUUUGACU AGUCAAAUU ACUUAGAG 974 CCUCUAAG CUGAUGA X GAA AAUUUGAC GUCAAAUUA CUUAGAGG 30 975 UGGCCUCU CUGAUGA X GAA AGUAAUUU AAAUUACUU AGAGGCCA 978 AUGGCCUC CUGAUGA X GAA AAGUAAUU AAUUACUUA GAGGCCAU 979

GACAAGAG CUGAUGA X GAA AUGGCCUC

	991	GAGGACAA	CUGAUGA	X	GAA	AGUAUGGC	GCCAUACUC	UUGUCCUC
	993	UUGAGGAC	CUGAUGA	X	GAA	AGAGUAUG	CAUACUCUU	GUCCUCAA
	996	CAAUUGAG	CUGAUGA	X	GAA	ACAAGAGU	ACUCUUGUC	CUCAAUUG
	999	GUACAAUU	CUGAUGA	X	GAA	AGGACAAG	CUUGUCCUC	AAUUGUAC
5	1003	AGCAGUAC	CUGAUGA	X	GAA	AUUGAGGA	UCCUCAAUU	GUACUGCU
	1006	GGUAGCAG	CUGAUGA	X	GAA	ACAAUUGA	UCAAUUGUA	CUGCUACC
	1012	GGGAGUGG	CUGAUGA	X	GAA	AGCAGUAC	GUACUGCUA	CCACUCCC
	1018	GUUCAAGG	CUGAUGA	X	GAA	AGUGGUAG	CUACCACUC	CCUUGAAC
	1022	UCGUGUUC	CUGAUGA	X	GAA	AGGGAGUG	CACUCCCUU	GAACACGA
10	1035	GUCAUUUG	CUGAUGA	X	GAA	ACUCUCGU	ACGAGAGUU	CAAAUGAC
	1036	GGUCAUUU	CUGAUGA	X	GAA	AACUCUCG	CGAGAGUUC	AAAUGACC
	1051	AUCAGGGU	CUGAUGA	X	GAA	ACUCCAGG	CCUGGAGUU	ACCCUGAU
	1052	CAUCAGGG	CUGAUGA	X	GAA	AACUCCAG	CUGGAGUUA	CCCUGAUG
	1069	AGCUCUCU	CUGAUGA	X	GAA	UUUUUUUA	AAAAAAAUA	AGAGAGCU
15	1078	CCUUACGG	CUGAUGA	X	GAA	AGCUCUCU	AGAGAGCUU	CCGUAAGG
	1079	GCCUUACG	CUGAUGA	X	GAA	AAGCUCUC	GAGAGCUUC	CGUAAGGC
	1083	CGUCGCCU	CUGAUGA	X	GAA	ACGGAAGC	GCUUCCGUA	AGGCGACG
	1095	CUUUGGUC	CUGAUGA	X	GAA	AUUCGUCG	CGACGAAUU	GACCAAAG
	1108	GGCAUGGG	CUGAUGA	X	GAA	AUUGCUUU	AAAGCAAUU	CCCAUGCC
20	1109	UGGCAUGG	CUGAUGA	X	GAA	AAUUGCUU	AAGCAAUUC	CCAUGCCA
	1122	CUGUAGAA	CUGAUGA	X	GAA	AUGUUGGC	GCCAACAUA	UUCUACAG
	1124	CACUGUAG	CUGAUGA	X	GAA	AUAUGUUG	CAACAUAUU	CUACAGUG
	1125	ACACUGUA	CUGAUGA	X	GAA	AAUAUGUU	AACAUAUUC	UACAGUGU
	1127	GAACACUG	CUGAUGA	X	GAA	AGAAUAUG	CAUAUUCUA	CAGUGUUC
25	1134	AUAGUAAG	CUGAUGA	X	GAA	ACACUGUA	UACAGUGUU	CUUACUAU
	1135	AAUAGUAA	CUGAUGA	X	GAA	AACACUGU	ACAGUGUUC	UUACUAUU
	1137	UCAAUAGU	CUGAUGA	X	GAA	AGAACACU	AGUGUUCUU	ACUAUUGA
	1138	GUCAAUAG	CUGAUGA	X	GAA	AAGAACAC	GUGUUCUUA	CUAUUGAC
	1141	UUUGUCAA	CUGAUGA	X	GAA	AGUAAGAA	UUCUUACUA	UUGACAAA
30	1143	AUUUUGUC	CUGAUGA	X	GAA	AUAGUAAG	CUUACUAUU	GACAAAAU
	1173	CAAGUAUA	CUGAUGA	X	GAA	AGUCCUUU	AAAGGACUU	UAUACUUG
	1174	ACAAGUAU	CUGAUGA	X	GAA	AAGUCCUU	AAGGACUUU	AUACUUGU
	1175	GACAAGUA	CUGAUGA	X	GAA	AAAGUCCU	ассасиниа	HACHIGHE

	1177	ACGACAAG	CUGAUGA	X	GAA	AUAAAGUC	GACUUUAUA	CUUGUCGU
	1180	UACACGAC	CUGAUGA	X	GAA	AGUAUAAA	UUUAUACUU	GUCGUGUA
	1183	CCUUACAC	CUGAUGA	X	GAA	ACAAGUAU	AUACUUGUC	GUGUAAGG
	1188	CCACUCCU	CUGAUGA	X	GAA	ACACGACA	UGUCGUGUA	AGGAGUGG
5	1202	AUUUGAAU	CUGAUGA	X	GAA	AUGGUCCA	UGGACCAUC	AUUCAAAU
	1205	CAGAUUUG	CUGAUGA	X	GAA	AUGAUGGU	ACCAUCAUU	CAAAUCUG
	1206	ACAGAUUU	CUGAUGA	X	GAA	AAUGAUGG	CCAUCAUUC	AAAUCUGU
	1211	UGUUAACA	CUGAUGA	X	GAA	AUUUGAAU	AUUCAAAUC	UGUUAACA
	1215	GAGGUGUU	CUGAUGA	X	GAA	ACAGAUUU	AAAUCUGUU	AACACCUC
10	1216	UGAGGUGU	CUGAUGA	X	GAA	AACAGAUU	AAUCUGUUA	ACACCUCA
	1223	UAUGCACU	CUGAUGA	X	GAA	AGGUGUUA	UAACACCUC	AGUGCAUA
	1231	AUCAUAUA	CUGAUGA	X	GAA	AUGCACUG	CAGUGCAUA	UAUAUGAU
	1233	UUAUCAUA	CUGAUGA	X	GAA	AUAUGCAC	GUGCAUAUA	UAUGAUAA
	1235	CUUUAUCA	CUGAUGA	X	GAA	AUAUAUGC	GCAUAUAUA	UGAUAAAG
15	1240	GAAUGCUU	CUGAUGA	X	GAA	AUCAUAUA	UAUAUGAUA	AAGCAUUC
	1247	CAGUGAUG	CUGAUGA	X	GAA	AUGCUUUA	UAAAGCAUU	CAUCACUG
	1248	ACAGUGAU	CUGAUGA	X	GAA	AAUGCUUU	AAAGCAUUC	AUCACUGU
	1251	UUCACAGU	CUGAUGA	X	GAA	AUGAAUGC	GCAUUCAUC	ACUGUGAA
	1264	CUGUUUUC	CUGAUGA	X	GAA	AUGUUUCA	UGAAACAUC	GAAAACAG
20	1281	ACGGUUUC	CUGAUGA	X	GAA	AGCACCUG	CAGGUGCUU	GAAACCGU
	1290	UUGCCAGC	CUGAUGA	X	GAA	ACGGUUUC	GAAACCGUA	GCUGGCAA
	1304	GCCGGUAA	CUGAUGA	X	GAA	ACCGCUUG	CAAGCGGUC	UUACCGGC
	1306	GAGCCGGU	CUGAUGA	X	GAA	AGACCGCU	AGCGGUCUU	ACCGGCUC
	1307	AGAGCCGG	CUGAUGA	X	GAA	AAGACCGC	GCGGUCUUA	CCGGCUCU
25	1314	UUCAUAGA	CUGAUGA	X	GAA	AGCCGGUA	UACCGGCUC	UCUAUGAA
	1316	CUUUCAUA	CUGAUGA	X	GAA	AGAGCCGG	CCGGCUCUC	UAUGAAAG
	1318	CACUUUCA	CUGAUGA	X	GAA	AGAGAGCC	GGCUCUCUA	UGAAAGUG
	1334	GCGAGGGA	CUGAUGA	X	GAA	AUGCCUUC	GAAGGCAUU	UCCCUCGC
	1335	GGCGAGGG	CUGAUGA	X	GAA	AAUGCCUU	AAGGCAUUU	CCCUCGCC
30	1336	CGGCGAGG	CUGAUGA	X	GAA	AAAUGCCU	AGGCAUUUC	CCUCGCCG
	1340	CUUCCGGC	CUGAUGA	X	GAA	AGGGAAAU	AUUUCCCUC	GCCGGAAG
	1350	AACCAUAC	CUGAUGA	X	GAA	ACUUCCGG	CCGGAAGUU	GUAUGGUU
	1353	ІППІВАССА	CUGALIGA	x	GAA	ΑΓΑΛΟΙΠΙΟ	СААСІПІСІТА	HCCHIAAA

	1358	CAUCUUUU	CUGAUGA	X	GAA	ACCAUACA	UGUAUGGUU	AAAAGAUG
	1359	CCAUCUUU	CUGAUGA	X	GAA	AACCAUAC	GUAUGGUU	AAAGAUGG
	1370	UCGCAGGU	CUGAUGA	X	GAA	ACCCAUCU	AGAUGGGUU	ACCUGCGA
	1371	GUCGCAGG	CUGAUGA	X	GAA	AACCCAUC	GAUGGGUUA	CCUGCGAC
5	1388	AGCGAGCA	CUGAUGA	X	GAA	AUUUCUCA	UGAGAAAU	ugcucgcu
	1393	CAAAUAGC	CUGAUGA	X	GAA	AGCAGAUU	AAUCUGCUG	GCUAUUUG
	1397	GAGUCAAA	CUGAUGA	X	GAA	AGCGAGCA	UGCUCGCUZ	UUUGACUC
	1399	ACGAGUCA	CUGAUGA	X	GAA	AUAGCGAG	CUCGCUAUL	UGACUCGU
	1400	CACGAGUC	CUGAUGA	X	GAA	AAUAGCGA	UCGCUAUUL	GACUCGUG
10	1405	GUAGCCAC	CUGAUGA	X	GAA	AGUCAAAU	AUUUGACU	GUGGCUAC
	1412	UUAACGAG	CUGAUGA	X	GAA	AGCCACGA	UCGUGGCUA	CUCGUUAA
	1415	UAAUUAAC	CUGAUGA	X	GAA	AGUAGCCA	UGGCUACUC	GUUAAUUA
	1418	UGAUAAUU	CUGAUGA	X	GAA	ACGAGUAG	CUACUCGUU	AAUUAUCA
	1419	UUGAUAAU	CUGAUGA	X	GAA	AACGAGUA	UACUCGUUZ	AUUAUCAA
15	1422	UCCUUGAU	CUGAUGA	X	GAA	AUUAACGA	UCGUUAAUI	AUCAAGGA
	1423	GUCCUUGA	CUGAUGA	X	GAA	AAUUAACG	CGUUAAUUA	UCAAGGAC
	1425	ACGUCCUU	CUGAUGA	X	GAA	AUAAUUAA	UUAAUUAUU	AAGGACGU
	1434	UCUUCAGU	CUGAUGA	X	GAA	ACGUCCUU	AAGGACGUA	ACUGAAGA
	1456	GAUUGUAU	CUGAUGA	X	GAA	AUUCCCUG	CAGGGAAU	AUACAAUC
20	1457	AGAUUGUA	CUGAUGA	X	GAA	AAUUCCCU	AGGGAAUU	UACAAUCU
	1459	CAAGAUUG	CUGAUGA	X	GAA	AUAAUUCC	GGAAUUAUA	CAAUCUUG
	1464	CUCAGCAA	CUGAUGA	X	GAA	AUUGUAUA	UAUACAAU	UUGCUGAG
	1466	UGCUCAGC	CUGAUGA	X	GAA	AGAUUGUA	UACAAUCUI	GCUGAGCA
	1476	GACUGUUU	CUGAUGA	X	GAA	AUGCUCAG	CUGAGCAU	AAACAGUC
25	1484	ACACAUUU	CUGAUGA	X	GAA	ACUGUUUU	AAAACAGU	AAAUGUGU
	1493	GGUUUUUA	CUGAUGA	X	GAA	ACACAUUU	AAAUGUGUU	UAAAAACC
	1494	AGGUUUUU	CUGAUGA	X	GAA	AACACAUU	AAUGUGUU	AAAAACCU
	1495	GAGGUUUU	CUGAUGA	X	GAA	AAACACAU	AUGUGUUU	AAAACCUC
	1503	GUGGCAGU	CUGAUGA	X	GAA	AGGUUUUU	AAAAACCU	ACUGCCAC
30	1513	GACAAUUA	CUGAUGA	X	GAA	AGUGGCAG	CUGCCACU	UAAUUGUC
	1515	UUGACAAU	CUGAUGA	X	GAA	AGAGUGGC	GCCACUCU	AUUGUCAA
	1518	ACAUUGAC	CUGAUGA	X	GAA	AUUAGAGU	ACUCUAAU	GUCAAUGU
	1521	UUCACAUU	CUGAUGA	X	GAA	ACAAUUAG	CUAAUUGU	AAUGUGAA

	1539	UUUUCGUA	CUGAUGA	X	GAA	AUCUGGGG	CCCCAGAUU	UACGAAAA
	1540	CUUUUCGU	CUGAUGA	X	GAA	AAUCUGGG	CCCAGAUUU	ACGAAAAG
	1541	CCUUUUCG	CUGAUGA	X	GAA	AAAUCUGG	CCAGAUUUA	CGAAAAGG
	1556	GAAACGAU	CUGAUGA	X	GAA	ACACGGCC	GGCCGUGUC	AUCGUUUC
5	1559	CUGGAAAC	CUGAUGA	X	GAA	AUGACACG	CGUGUCAUC	GUUUCCAG
	1562	GGUCUGGA	CUGAUGA	X	GAA	ACGAUGAC	GUCAUCGUU	UCCAGACC
	1563	GGGUCUGG	CUGAUGA	X	GAA	AACGAUGA	UCAUCGUUU	CCAGACCC
	1564	CGGGUCUG	CUGAUGA	X	GAA	AAACGAUG	CAUCGUUUC	CAGACCCG
	1576	UGGGUAGA	CUGAUGA	X	GAA	AGCCGGGU	ACCCGGCUC	UCUACCCA
LO	1578	AGUGGGUA	CUGAUGA	X	GAA	AGAGCCGG	CCGGCUCUC	UACCCACU
	1580	CCAGUGGG	CUGAUGA	X	GAA	AGAGAGCC	GGCUCUCUA	CCCACUGG
	1602	CAAGUCAG	CUGAUGA	X	GAA	AUUUGUCU	AGACAAAUC	CUGACUUG
	1609	UGCGGUAC	CUGAUGA	X	GAA	AGUCAGGA	UCCUGACUU	GUACCGCA
	1612	AUAUGCGG	CUGAUGA	X	GAA	ACAAGUCA	UGACUUGUA	CCGCAUAU
15	1619	GGAUACCA	CUGAUGA	X	GAA	AUGCGGUA	UACCGCAUA	UGGUAUCC
	1624	UUGAGGGA	CUGAUGA	X	GAA	ACCAUAUG	CAUAUGGUA	UCCCUCAA
	1626	GGUUGAGG	CUGAUGA	X	GAA	AUACCAUA	UAUGGUAUC	CCUCAACC
	1630	UGUAGGUU	CUGAUGA	X	GAA	AGGGAUAC	GUAUCCCUC	AACCUACA
	1636	CUUGAUUG	CUGAUGA	X	GAA	AGGUUGAG	CUCAACCUA	CAAUCAAG
20	1641	AACCACUU	CUGAUGA	X	GAA	AUUGUAGG	CCUACAAUC	AAGUGGUU
	1649	GGUGCCAG	CUGAUGA	X	GAA	ACCACUUG	CAAGUGGUU	CUGGCACC
	1650	GGGUGCCA	CUGAUGA	X	GAA	AACCACUU	AAGUGGUUC	UGGCACCC
	16 63	AUUAUGGU	CUGAUGA	X	GAA	ACAGGGGU	ACCCCUGUA	ACCAUAAU
	1669	GGAAUGAU	CUGAUGA	X	GAA	AUGGUUAC	GUAACCAUA	AUCAUUCC
25	1672	UUCGGAAU	CUGAUGA	X	GAA	AUUAUGGU	ACCAUAAUC	AUUCCGAA
	1675	UGCUUCGG	CUGAUGA	X	GAA	AUGAUUAU	AUAAUCAUU	CCGAAGCA
	1676	UUGCUUCG	CUGAUGA	X	GAA	AAUGAUUA	UAAUCAUUC	CGAAGCAA
	1694	UGGAACAA	CUGAUGA	X	GAA	AGUCACAC	GUGUGACUU	UUGUUCCA
	1695	UUGGAACA	CUGAUGA	X	GAA	AAGUCACA	UGUGACUUU	UGUUCCAA
30	1696	AUUGGAAC	CUGAUGA	X	GAA	AAAGUCAC	GUGACUUUU	GUUCCAAU
	1699	AUUAUUGG	CUGAUGA	X	GAA	ACAAAAGU	ACUUUUGUU	CCAAUAAU
	1700	CAUUAUUG	CUGAUGA	X	GAA	AACAAAAG	CUUUUGUUC	CAAUAAUG
	1705	CUCUUCAU	CUGAUGA	Х	GAA	AUUGGAAC	GUUCCAAUA	AUGAAGAG

	1715	GGAUAAAG	CUGAUGA	X	GAA	ACUCUUCA	UGAAGAGUC	CUUUAUCC
	1718	CCAGGAUA	CUGAUGA	X	GAA	AGGACUCU	AGAGUCCUU	UAUCCUGG
	1719	UCCAGGAU	CUGAUGA	X	GAA	AAGGACUC	GAGUCCUUU	AUCCUGGA
	1720	AUCCAGGA	CUGAUGA	X	GAA	AAAGGACU	AGUCCUUUA	UCCUGGAU
5	1722	GCAUCCAG	CUGAUGA	X	GAA	AUAAAGGA	UCCUUUAUC	CUGGAUGC
	1755	AUGCUCUC	CUGAUGA	X	GAA	AUUCUGUU	AACAGAAUU	GAGAGCAU
	1764	CGCUGAGU	CUGAUGA	x	GAA	AUGCUCUC	GAGAGCAUC	ACUCAGCG
	1768	CAUGCGCU	CUGAUGA	X	GAA	AGUGAUGC	GCAUCACUC	AGCGCAUG
	1782	CCUUCUAU	CUGAUGA	X	GAA	AUUGCCAU	AUGGCAAUA	AUAGAAGG
10	1785	υυυςςυυς	CUGAUGA	X	GAA	AUUAUUGC	GCAAUAAUA	GAAGGAAA
	1798	AGCCAUCU	CUGAUGA	X	GAA	AUUCUUUC	GAAAGAAUA	AGAUGGCU
	1807	CAAGGUGC	CUGAUGA	X	GAA	AGCCAUCU	AGAUGGCUA	GCACCUUG
	1814	CCACAACC	CUGAUGA	X	GAA	AGGUGCUA	UAGCACCUU	GGUUGUGG
	1818	UCAGCCAC	CUGAUGA	X	GAA	ACCAAGGU	ACCUUGGUU	GUGGCUGA
15	1829	AAAUUCUA	CUGAUGA	X	GAA	AGUCAGCC	GGCUGACUC	UAGAAUUU
	1831	AGAAAUUC	CUGAUGA	X	GAA	AGAGUCAG	CUGACUCUA	GAAUUUCU
	1836	AUUCCAGA	CUGAUGA	X	GAA	AUUCUAGA	UCUAGAAUU	UCUGGAAU
	1837	GAUUCCAG	CUGAUGA	X	GAA	AAUUCUAG	CUAGAAUUU	CUGGAAUC
	1838	AGAUUCCA	CUGAUGA	X	GAA	AAAUUCUA	UAGAAUUUC	UGGAAUCU
20	1845	CAAAUGUA	CUGAUGA	X	GAA	AUUCCAGA	UCUGGAAUC	UACAUUUG
	1847	UGCAAAUG	CUGAUGA	X	GAA	AGAUUCCA	UGGAAUCUA	CAUUUGCA
	1851	GCUAUGCA	CUGAUGA	X	GAA	AUGUAGAU	AUCUACAUU	UGCAUAGC
	1852	AGCUAUGC	CUGAUGA	X	GAA	AAUGUAGA	UCUACAUUU	GCAUAGCU
	1857	UUGGAAGC	CUGAUGA	X	GAA	AUGCAAAU	AUUUGCAUA	GCUUCCAA
25	1861	UUUAUUGG	CUGAUGA	X	GAA	AGCUAUGC	GCAUAGCUU	CCAAUAAA
	1862	CUUUAUUG	CUGAUGA	X	GAA	AAGCUAUG	CAUAGCUUC	CAAUAAAG
	1867	CCCAACUU	CUGAUGA	X	GAA	AUUGGAAG	CUUCCAAUA	AAGUUGGG
	1872	ACAGUCCC	CUGAUGA	X	GAA	ACUUUAUU	AAUAAAGUU	GGGACUGU
	1893	UAAAAGCU	CUGAUGA	X	GAA	AUGUUUCU	AGAAACAUA	AGCUUUUA
30	1898	UGAUAUAA	CUGAUGA	x	GAA	AGCUUAUG	CAUAAGCUU	UUAUAUCA
	1899	GUGAUAUA	CUGAUGA	x	GAA	AAGCUUAU	AUAAGCUUU	UAUAUCAC
	1900	UGUGAUAU	CUGAUGA	X	GAA	AAAGCUUA	UAAGCUUUU	AUAUCACA
	1901	CUGUGAUA	CUGAUGA	x	GAA	AAAAGCUU	AAGCUUUUA	UAUCACAG

	1903	AUCUGUGA	CUGAUGA	X	GAA	AUAAAAGC	GCUUUUAUA	UCACAGAU
	1905	ACAUCUGU	CUGAUGA	X	GAA	AUAUAAA	UUUUAUAUC	ACAGAUGU
	1925	UAACAUGA	CUGAUGA	X	GAA	ACCCAUUU	AAAUGGGUU	UCAUGUUA
	1926	UUAACAUG	CUGAUGA	X	GAA	AACCCAUU	AAUGGGUUU	CAUGUUAA
5	1927	GUUAACAU	CUGAUGA	X	GAA	AAACCCAU	AUGGGUUUC	AUGUUAAC
	1932	UCCAAGUU	CUGAUGA	X	GAA	ACAUGAAA	UUUCAUGUU	AACUUGGA
	1933	UUCCAAGU	CUGAUGA	x	GAA	AACAUGAA	UUCAUGUUA	ACUUGGAA
	1937	υυυυυυ	CUGAUGA	X	GAA	AGUUAACA	UGUUAACUU	GGAAAAA
	1976	CUGUGCAA	CUGAUGA	X	GAA	ACAGUUUC	GAAACUGUC	UUGCACAG
10	1978	AACUGUGC	CUGAUGA	X	GAA	AGACAGUU	AACUGUCUU	GCACAGUU
	1986	AACUUGUU	CUGAUGA	X	GAA	ACUGUGCA	UGCACAGUU	AACAAGUU
	1987	GAACUUGU	CUGAUGA	X	GAA	AACUGUGC	GCACAGUUA	ACAAGUUC
	1994	UGUAUAAG	CUGAUGA	X	GAA	ACUUGUUA	UAACAAGUU	CUUAUACA
	1995	CUGUAUAA	CUGAUGA	X	GAA	AACUUGUU	AACAAGUUC	UUAUACAG
15	1997	CUCUGUAU	CUGAUGA	X	GAA	AGAACUUG	CAAGUUCUU	AUACAGAG
	1998	UCUCUGUA	CUGAUGA	X	GAA	AAGAACUU	AAGUUCUUA	UACAGAGA
	2000	CGUCUCUG	CUGAUGA	X	GAA	AUAAGAAC	GUUCUUAUA	CAGAGACG
	2010	AUCCAAGU	CUGAUGA	X	GAA	ACGUCUCU	AGAGACGUU	ACUUGGAU
	2011	AAUCCAAG	CUGAUGA	X	GAA	AACGUCUC	GAGACGUUA	CUUGGAUU
20	2014	UAAAAUCC	CUGAUGA	X	GAA	AGUAACGU	ACGUUACUU	GGAUUUUA
	2019	CGCAGUAA	CUGAUGA	X	GAA	AUCCAAGU	ACUUGGAUU	UUACUGCG
	2020	CCGCAGUA	CUGAUGA	X	GAA	AAUCCAAG	CUUGGAUUU	UACUGCGG
	2021	UCCGCAGU	CUGAUGA	X	GAA	AAAUCCAA	UUGGAUUUU	ACUGCGGA
	2022	GUCCGCAG	CUGAUGA	X	GAA	AAAAUCCA	UGGAUUUUA	CUGCGGAC
25	2034	CUGUUAUU	CUGAUGA	X	GAA	ACUGUCCG	CGGACAGUU	AAUAACAG
	2035	UCUGUUAU	CUGAUGA	X	GAA	AACUGUCC	GGACAGUUA	AUAACAGA
	2038	UGUUCUGU	CUGAUGA	X	GAA	AUUAACUG	CAGUUAAUA	ACAGAACA
	2054	UAAUACUG	CUGAUGA	X	GAA	AGUGCAUU	AAUGCACUA	CAGUAUUA
	2059	CUUGCUAA	CUGAUGA	X	GAA	ACUGUAGU	ACUACAGUA	UUAGCAAG
30	2061	UGCUUGCU	CUGAUGA	X	GAA	AUACUGUA	UACAGUAUU	AGCAAGCA
	2062	UUGCUUGC	CUGAUGA	X	GAA	AAUACUGU	ACAGUAUUA	GCAAGCAA
	2082	UCCUUAGU	CUGAUGA	X	GAA	AUGGCCAU	AUGGCCAUC	ACUAAGGA
	2086	GUGCUCCU	CUGAUGA	Х	GAA	AGUGAUGG	CCAUCACUA	AGGAGCAC

	2096	GAGUGAUG	CUGAUGA	X	GAA	AGUGCUCC	GGAGCACUC	CAUCACUC
	2100	UUAAGAGU	CUGAUGA	X	GAA	AUGGAGUG	CACUCCAUC	ACUCUUAA
	2104	AAGAUUAA	CUGAUGA	X	GAA	AGUGAUGG	CCAUCACUC	UUAAUCUU
	2106	GUAAGAUU	CUGAUGA	X	GAA	AGAGUGAU	AUCACUCUU	AAUCUUAC
5	2107	GGUAAGAU	CUGAUGA	X	GAA	AAGAGUGA	UCACUCUUA	AUCUUACC
	2110	GAUGGUAA	CUGAUGA	X	GAA	AUUAAGAG	CUCUUAAUC	UUACCAUC
	2112	AUGAUGGU	CUGAUGA	X	GAA	AGAUUAAG	CUUAAUCUU	ACCAUCAU
	2113	CAUGAUGG	CUGAUGA	X	GAA	AAGAUUAA	UUAAUCUUA	CCAUCAUG
	2118	ACAUUCAU	CUGAUGA	X	GAA	AUGGUAAG	CUUACCAUC	AUGAAUGU
10	2127	UGCAGGGA	CUGAUGA	X	GAA	ACAUUCAU	AUGAAUGUU	UCCCUGCA
	2128	UUGCAGGG	CUGAUGA	X	GAA	AACAUUCA	UGAAUGUUU	CCCUGCAA
	2129	CUUGCAGG	CUGAUGA	X	GAA	AAACAUUC	GAAUGUUUC	CCUGCAAG
	2140	GGUGCCUG	CUGAUGA	X	GAA	AUCUUGCA	UGCAAGAUU	CAGGCACC
	2141	AGGUGCCU	CUGAUGA	X	GAA	AAUCUUGC	GCAAGAUUC	AGGCACCU
15	2150	UGCAGGCA	CUGAUGA	X	GAA	AGGUGCCU	AGGCACCUA	UGCCUGCA
	2172	CCUGUGUA	CUGAUGA	X	GAA	ACAUUCCU	AGGAAUGUA	UACACAGG
	2174	CCCCUGUG	CUGAUGA	X	GAA	AUACAUUC	GAAUGUAUA	CACAGGGG
	2190	UUCUGGAG	CUGAUGA	X	GAA	AUUUCUUC	GAAGAAAUC	CUCCAGAA
	2193	UUCUUCUG	CUGAUGA	X	GAA	AGGAUUUC	GAAAUCCUC	CAGAAGAA
20	2208	CUGAUUGU	CUGAUGA	X	GAA	AUUUCUUU	AAAGAAAUU	ACAAUCAG
	2209	UCUGAUUG	CUGAUGA	X	GAA	AAUUUCUU	AAGAAAUUA	CAAUCAGA
	2214	UGAUCUCU	CUGAUGA	X	GAA	AUUGUAAU	AUUACAAUC	AGAGAUCA
	2221	UGCUUCCU	CUGAUGA	X	GAA	AUCUCUGA	UCAGAGAUC	AGGAAGCA
	2234	GCAGGAGG	CUGAUGA	X	GAA	AUGGUGCU	AGCACCAUA	CCUCCUGC
25	2238	UUUCGCAG	CUGAUGA	X	GAA	AGGUAUGG	CCAUACCUC	CUGCGAAA
	2250	UGAUCACU	CUGAUGA	X	GAA	AGGUUUCG	CGAAACCUC	AGUGAUCA
	2257	CACUGUGU	CUGAUGA	X	GAA	AUCACUGA	UCAGUGAUC	ACACAGUG
	2271	GAACUGCU	CUGAUGA	X	GAA	AUGGCCAC	GUGGCCAUC	AGCAGUUC
	2278	AGUGGUGG	CUGAUGA	X	GAA	ACUGCUGA	UCAGCAGUU	CCACCACU
30	2279	AAGUGGUG	CUGAUGA	X	GAA	AACUGCUG	CAGCAGUUC	CACCACUU
	2287	ACAGUCUA	CUGAUGA	X	GAA	AGUGGUGG	CCACCACUU	UAGACUGU
	2288	GACAGUCU	CUGAUGA	X	GAA	AAGUGGUG	CACCACUUU	AGACUGUC
	2289	UGACAGUC	CUGAUGA	X	GAA	AAAGUGGU	ACCACUUUA	GACUGUCA

PCT/US96/17480

WO 97/15662

	2296	AUUAGCAU	CUGAUGA	X	GAA	ACAGUCUA	UAGACUGUC	AUGCUAAU
	2302	GACACCAU	CUGAUGA	X	GAA	AGCAUGAC	GUCAUGCUA	AUGGUGUC
	2310	GGCUCGGG	CUGAUGA	X	GAA	ACACCAUU	AAUGGUGUC	CCCGAGCC
	2320	AGUGAUCU	CUGAUGA	x	GAA	AGGCUCGG	CCGAGCCUC	AGAUCACU
5	2325	AACCAAGU	CUGAUGA	X	GAA	AUCUGAGG	CCUCAGAUC	ACUUGGUU
	2329	UUUAAACC	CUGAUGA	X	GAA	AGUGAUCU	AGAUCACUU	GGUUUAAA
	2333	UGUUUUUA	CUGAUGA	X	GAA	ACCAAGUG	CACUUGGUU	UAAAAACA
	2334	UUGUUUUU	CUGAUGA	X	GAA	AACCAAGU	ACUUGGUUU	AAAAACAA
	2335	GUUGUUUU	CUGAUGA	X	GAA	AAACCAAG	CUUGGUUUA	AAAACAAC
10	2352	UCUUGUUG	CUGAUGA	X	GAA	AUUUUGUG	CACAAAAUA	CAACAAGA
	2370	CCUAAAAU	CUGAUGA	X	GAA	AUUCCAGG	CCUGGAAUU	AUUUUAGG
	2371	UCCUAAAA	CUGAUGA	X	GAA	AAUUCCAG	CUGGAAUUA	UUUUAGGA
	2373	GGUCCUAA	CUGAUGA	X	GAA	AUAAUUCC	GGAAUUAUU	UUAGGACC
	2374	UGGUCCUA	CUGAUGA	X	GAA	AAUAAUUC	GAAUUAUUU	UAGGACCA
15	2375	CUGGUCCU	CUGAUGA	X	GAA	UUAAUAAA	AAUUAUUUU	AGGACCAG
	2376	CCUGGUCC	CUGAUGA	X	GAA	AAAAUAAU	AUUUUUUA	GGACCAGG
	2399	UUUCAAUA	CUGAUGA	X	GAA	ACAGCGUG	CACGCUGUU	UAUUGAAA
	2400	CUUUCAAU	CUGAUGA	X	GAA	AACAGCGU	ACGCUGUUU	AUUGAAAG
	2401	UCUUUCAA	CUGAUGA	X	GAA	AAACAGCG	CGCUGUUUA	UUGAAAGA
20	2403	ACUCUUUC	CUGAUGA	X	GAA	AUAAACAG	CUGUUUAUU	GAAAGAGU
	2412	ucuucugu	CUGAUGA	X	GAA	ACUCUUUC	GAAAGAGUC	ACAGAAGA
	2433	CAGUGAUA	CUGAUGA	X	GAA	ACACCUUC	GAAGGUGUC	UAUCACUG
	2435	UGCAGUGA	CUGAUGA	X	GAA	AGACACCU	AGGUGUCUA	UCACUGCA
	2437	UUUGCAGU	CUGAUGA	X	GAA	AUAGACAC	GUGUCUAUC	ACUGCAAA
25	2465	UUUCCACA	CUGAUGA	X	GAA	AGCCCUUC	GAAGGGCUC	UGUGGAAA
	2476	GUAUGCUG	CUGAUGA	X	GAA	ACUUUCCA	UGGAAAGUU	CAGCAUAC
	2477	GGUAUGCU	CUGAUGA	X	GAA	AACUUUCC	GGAAAGUUC	AGCAUACC
	2483	CAGUGAGG	CUGAUGA	X	GAA	AUGCUGAA	UUCAGCAUA	CCUCACUG
	2487	UGAACAGU	CUGAUGA	X	GAA	AGGUAUGC	GCAUACCUC	ACUGUUCA
30	2493	GUUCCUUG	CUGAUGA	X	GAA	ACAGUGAG	CUCACUGUU	CAAGGAAC
	2494	GGUUCCUU	CUGAUGA	X	GAA	AACAGUGA	UCACUGUUC	AAGGAACC
	2504	ACUUGUCC	CUGAUGA	X	GAA	AGGUUCCU	AGGAACCUC	GGACAAGU
	2513	CCAGAUUA	CUGAUGA	X	GAA	ACUUGUCC	GGACAAGUC	UAAUCUGG

	2515	CUCCAGAII	כווכאווכא	Y	CAA	AGACUUGU	ACAAGUCUA	AUGUCCAC
	2518					AUUAGACU	AGUCUAAUC	
	2529					AUCAGCUC	GAGCUGAUC	
	2533					AGUGAUCA	UGAUCACUC	UAACAUGC
5	2535					AGAGUGAU	AUCACUCUA	
	2560	CCAGAAGA	CUGAUGA	X	GAA	AGUCGCAG	CUGCGACUC	UCUUCUGG
	2562	AGCCAGAA	CUGAUGA	X	GAA	AGAGUCGC	GCGACUCUC	UUCUGGCU
	2564	GGAGCCAG	CUGAUGA	X	GAA	AGAGAGUC	GACUCUCUU	CUGGCUCC
	2565	AGGAGCCA	CUGAUGA	X	GAA	AAGAGAGU	ACUCUCUUC	UGGCUCCU
10	2571	GUUAAUAG	CUGAUGA	X	GAA	AGCCAGAA	UUCUGGCUC	CUAUUAAC
	2574	AGGGUUAA	CUGAUGA	X	GAA	AGGAGCCA	UGGCUCCUA	UUAACCCU
	2576	GGAGGGUU	CUGAUGA	X	GAA	AUAGGAGC	GCUCCUAUU	AACCCUCC
	2577	AGGAGGGU	CUGAUGA	X	GAA	AAUAGGAG	CUCCUAUUA	ACCCUCCU
	2583	CGGAUAAG	CUGAUGA	X	GAA	AGGGUUAA	UUAACCCUC	CUUAUCCG
15	2586	UUUCGGAU	CUGAUGA	X	GAA	AGGAGGGU	ACCCUCCUU	AUCCGAAA
	2587	UUUUCGGA	CUGAUGA	X	GAA	AAGGAGGG	CCCUCCUUA	UCCGAAAA
	2589	AUUUUUCG	CUGAUGA	X	GAA	AUAAGGAG	CUCCUUAUC	CGAAAAAU
	2606	CAGAAGAA	CUGAUGA	x	GAA	ACCUUUUC	GAAAAGGUC	UUCUUCUG
	2608	UUCAGAAG	CUGAUGA	X	GAA	AGACCUUU	AAAGGUCUU	CUUCUGAA
20	2609	UUUCAGAA	CUGAUGA	X	GAA	AAGACCUU	AAGGUCUUC	UUCUGAAA
	2611	UAUUUCAG	CUGAUGA	X	GAA	AGAAGACC	GGUCUUCUU	CUGAAAUA
	2612	UUAUUUCA	CUGAUGA	X	GAA	AAGAAGAC	GUCUUCUUC	UGAAAUAA
	2619	UCAGUCUU	CUGAUGA	X	GAA	AUUUCAGA	UCUGAAAUA	AAGACUGA
	2630	UUGAUAGG	CUGAUGA	X	GAA	AGUCAGUC	GACUGACUA	CCUAUCAA
25	2634	AUAAUUGA	CUGAUGA	X	GAA	AGGUAGUC	GACUACCUA	UCAAUUAU
	2636	UUAUAAUU	CUGAUGA	X	GAA	AUAGGUAG	CUACCUAUC	AAUUAUAA
	2640	UCCAUUAU	CUGAUGA	X	GAA	AUUGAUAG	CUAUCAAUU	AUAAUGGA
	2641	GUCCAUUA	CUGAUGA	X	GAA	AAUUGAUA	UAUCAAUUA	UAAUGGAC
	2643	GGGUCCAU	CUGAUGA	X	GAA	AUAAUUGA	UCAAUUAUA	AUGGACCC
30	2661	UCCAAAGG	CUGAUGA	x	GAA	ACUUCAUC	GAUGAAGUU	CCUUUGGA
	2662	AUCCAAAG	CUGAUGA	X	GAA	AACUUCAU	AUGAAGUUC	CUUUGGAU
	2665	CUCAUCCA	CUGAUGA	x	GAA	AGGAACUU	AAGUUCCUU	UGGAUGAG
	2666	GCUCAUCC	CUGAUGA	x	GAA	AAGGAACU	AGUUCCUUU	GGAUGAGC

	2688	UCAUAAGG	CUGAUGA	X	GAA	AGCCGCUC	GAGCGGCUC	CCUUAUGA
	2692	GGCAUCAU	CUGAUGA	X	GAA	AGGGAGCC	GGCUCCCUU	AUGAUGCC
	2693	UGGCAUCA	CUGAUGA	X	GAA	AAGGGAGC	GCUCCCUUA	UGAUGCCA
	2714	CCCGGGCA	CUGAUGA	X	GAA	ACUCCCAC	GUGGGAGUU	UGCCCGGG
5	2715	UCCCGGGC	CUGAUGA	X	GAA	AACUCCCA	UGGGAGUUU	GCCCGGGA
	2730	CCCAGUUU	CUGAUGA	X	GAA	AGUCUCUC	GAGAGACUU	AAACUGGG
	2731	GCCCAGUU	CUGAUGA	X	GAA	AAGUCUCU	AGAGACUUA	AACUGGGC
	2744	UUCCAAGU	CUGAUGA	X	GAA	AUUUGCCC	GGGCAAAUC	ACUUGGAA
	2748	CCUCUUCC	CUGAUGA	X	GAA	AGUGAUUU	AAAUCACUU	GGAAGAGG
10	2761	UUUUCCAA	CUGAUGA	X	GAA	AGCCCCUC	GAGGGGCUU	UUGGAAAA
	2762	CUUUUCCA	CUGAUGA	X	GAA	AAGCCCCU	AGGGGCUUU	UGGAAAAG
	2763	ACUUUUCC	CUGAUGA	X	GAA	AAAGCCCC	GGGGCUUUU	GGAAAAGU
	2775	GAUGCUUG	CUGAUGA	X	GAA	ACCACUUU	AAAGUGGUU	CAAGCAUC
	2 7 76	UGAUGCUU	CUGAUGA	X	GAA	AACCACUU	AAGUGGUUC	AAGCAUCA
15	2783	CAAAUGCU	CUGAUGA	X	GAA	AUGCUUGA	UCAAGCAUC	AGCAUUUG
	2789	UAAUGCCA	CUGAUGA	X	GAA	AUGCUGAU	AUCAGCAUU	UGGCAUUA
	2790	UUAAUGCC	CUGAUGA	X	GAA	AAUGCUGA	UCAGCAUUU	GGCAUUAA
	2796	GAUUUCUU	CUGAUGA	X	GAA	AUGCCAAA	UUUGGCAUU	AAGAAAUC
	2797	UGAUUUCU	CUGAUGA	X	GAA	AAUGCCAA	UUGGCAUUA	AGAAAUCA
20	2804	ACGUAGGU	CUGAUGA	X	GAA	AUUUCUUA	UAAGAAAUC	ACCUACGU
	2809	CCGGCACG	CUGAUGA	X	GAA	AGGUGAUU	AAUCACCUA	CGUGCCGG
	2864	GAGCUUUG	CUGAUGA	X	GAA	ACUCGCUG	CAGCGAGUA	CAAAGCUC
	2872	AGUCAUCA	CUGAUGA	X	GAA	AGCUUUGU	ACAAAGCUC	UGAUGACU
	2886	AAGAUUUU	CUGAUGA	X	GAA	AGCUCAGU	ACUGAGCUA	AAAAUCUU
25	2892	UGGGUCAA	CUGAUGA	X	GAA	AUUUUUAG	CUAAAAAUC	UUGACCCA
	2894	UGUGGGUC	CUGAUGA	X	GAA	AGAUUUUU	AAAAAUCUU	GACCCACA
	2904	UGGUGGCC	CUGAUGA	X	GAA	AUGUGGGU	ACCCACAUU	GGCCACCA
	2914	CACGUUCA	CUGAUGA	X	GAA	AUGGUGGC	GCCACCAUC	UGAACGUG
	2925	AGCAGGUU	CUGAUGA	X	GAA	ACCACGUU	AACGUGGUU	AACCUGCU
30	2926	CAGCAGGU	CUGAUGA	X	GAA	AACCACGU	ACGUGGUUA	ACCUGCUG
	2962	CACCAUCA	CUGAUGA	X	GAA	AGGCCCUC	GAGGGCCUC	UGAUGGUG
	2973	UAUUCAAC	CUGAUGA	X	GAA	AUCACCAU	AUGGUGAUU	GUUGAAUA
	2976	CAGUAUUC	CUGAUGA	X	GAA	ACAAUCAC	GUGAUUGUU	GAAUACUG

	2981	AUUUGCAG	CUGAUGA	X	GAA	AUUCAACA	UGUUGAAUA	CUGCAAAU
	2990	GAUUUCCA	CUGAUGA	X	GAA	AUUUGCAG	CUGCAAAUA	UGGAAAUC
	2998	GUUGGAGA	CUGAUGA	X	GAA	AUUUCCAU	AUGGAAAUC	UCUCCAAC
	3000	UAGUUGGA	CUGAUGA	X	GAA	AGAUUUCC	GGAAAUCUC	UCCAACUA
5	3002	GGUAGUUG	CUGAUGA	X	GAA	AGAGAUUU	AAAUCUCUC	CAACUACC
	3008	UCUUGAGG	CUGAUGA	X	GAA	AGUUGGAG	CUCCAACUA	CCUCAAGA
	3012	UUGCUCUU	CUGAUGA	X	GAA	AGGUAGUU	AACUACCUC	AAGAGCAA
	3029	GAAAAAAU	CUGAUGA	X	GAA	AGUCACGU	ACGUGACUU	AUUUUUUC
	3030	AGAAAAA	CUGAUGA	X	GAA	AAGUCACG	CGUGACUUA	ບບບບບບບ
10	3032	UGAGAAAA	CUGAUGA	X	GAA	AUAAGUCA	UGACUUAUU	UUUUCUCA
	3033	UUGAGAAA	CUGAUGA	X	GAA	AAUAAGUC	GACUUAUUU	UUUCUCAA
	3034	GUUGAGAA	CUGAUGA	X	GAA	AAAUAAGU	ACUUAUUUU	UUCUCAAC
	3035	UGUUGAGA	CUGAUGA	X	GAA	AAAAUAAG	CUUAUUUUU	UCUCAACA
	3036	UUGUUGAG	CUGAUGA	X	GAA	AAAAAUAA	UUUUUUUAUU	CUCAACAA
15	3037	CUUGUUGA	CUGAUGA	X	GAA	AAAAAAUA	UAUUUUUUC	UCAACAAG
	3039	UCCUUGUU	CUGAUGA	X	GAA	AGAAAAA	nnnnncnc	AACAAGGA
	3057	UCCAUGUG	CUGAUGA	X	GAA	AGUGCUGC	GCAGCACUA	CACAUGGA
	3070	ບບດກຸດດາ	CUGAUGA	X	GAA	AGGCUCCA	UGGAGCCUA	AGAAAGAA
	3120	ACGCUAUC	CUGAUGA	X	GAA	AGUCUUGG	CCAAGACUA	GAUAGCGU
20	3124	GGUGACGC	CUGAUGA	X	GAA	AUCUAGUC	GACUAGAUA	GCGUCACC
	3129	CUGCUGGU	CUGAUGA	X	GAA	ACGCUAUC	GAUAGCGUC	ACCAGCAG
	3146	AGCUCGCA	CUGAUGA	X	GAA	AGCUUUCG	CGAAAGCUU	UGCGAGCU
	3147	GAGCUCGC	CUGAUGA	X	GAA	AAGCUUUC	GAAAGCUUU	GCGAGCUC
	3155	GAAAGCCG	CUGAUGA	X	GAA	AGCUCGCA	UGCGAGCUC	CGGCUUUC
2 5	3161	CUUCCUGA	CUGAUGA	X	GAA	AGCCGGAG	CUCCGGCUU	UCAGGAAG
	3162	UCUUCCUG	CUGAUGA	X	GAA	AAGCCGGA	UCCGGCUUU	CAGGAAGA
	3163	AUCUUCCU	CUGAUGA	X	GAA	AAAGCCGG	CCGGCUUUC	AGGAAGAU
	3172	CAGACUUU	CUGAUGA	X	GAA	AUCUUCCU	AGGAAGAUA	AAAGUCUG
	3178	AUCACUCA	CUGAUGA	X	GAA	ACUUUUAU	AUAAAAGUC	UGAGUGAU
30	3189	ucuuccuc	CUGAUGA	X	GAA	ACAUCACU	AGUGAUGUU	GAGGAAGA
	3205	ACCGUCAG	CUGAUGA	X	GAA	AUCCUCCU	AGGAGGAUU	CUGACGGU
	3206	AACCGUCA	CUGAUGA	X	GAA	AAUCCUCC	GGAGGAUUC	UGACGGUU
	3214	CUUGUAGA	CUGAUGA	X	GAA	ACCGUCAG	CUGACGGUU	UCUACAAG

	3215	CCUUGUAG	CUGAUGA	А	GAA	AACCGUCA	UGACGGUUU	CUACAAGG
	3216	UCCUUGUA	CUGAUGA	X	GAA	AAACCGUC	GACGGUUUC	UACAAGGA
	3218	GCUCCUUG	CUGAUGA	X	GAA	AGAAACCG	CGGUUUCUA	CAAGGAGC
	3231	UCCAUAGU	CUGAUGA	X	GAA	AUGGGCUC	GAGCCCAUC	ACUAUGGA
5	3235	AUCUUCCA	CUGAUGA	X	GAA	AGUGAUGG	CCAUCACUA	UGGAAGAU
	3244	AGAAAUCA	CUGAUGA	X	GAA	AUCUUCCA	UGGAAGAUC	UGAUUUCU
	3249	CUGUAAGA	CUGAUGA	X	GAA	AUCAGAUC	GAUCUGAUU	UCUUACAG
	3250	ACUGUAAG	CUGAUGA	X	GAA	AAUCAGAU	AUCUGAUUU	CUUACAGU
	3251	AACUGUAA	CUGAUGA	X	GAA	AAAUCAGA	UCUGAUUUC	UUACAGUU
LO	325 3	AAAACUGU	CUGAUGA	X	GAA	AGAAAUCA	UGAUUUCUU	ACAGUUUU
	3254	GAAAACUG	CUGAUGA	X	GAA	AAGAAAUC	GAUUUCUUA	CAGUUUUC
	3259	CACUUGAA	CUGAUGA	X	GAA	ACUGUAAG	CUUACAGUU	UUCAAGUG
	3260	CCACUUGA	CUGAUGA	X	GAA	AACUGUAA	UUACAGUUU	UCAAGUGG
	3261	GCCACUUG	CUGAUGA	X	GAA	AAACUGUA	UACAGUUUU	CAAGUGGC
15	3262	GGCCACUU	CUGAUGA	X	GAA	AAAACUGU	ACAGUUUUC	AAGUGGCC
	3284	AAGACAGG	CUGAUGA	X	GAA	ACUCCAUG	CAUGGAGUU	CCUGUCUU
	3285	GAAGACAG	CUGAUGA	X	GAA	AACUCCAU	AUGGAGUUC	CUGUCUUC
	3290	UUCUGGAA	CUGAUGA	X	GAA	ACAGGAAC	GUUCCUGUC	UUCCAGAA
	3292	CUUUCUGG	CUGAUGA	X	GAA	AGACAGGA	uccugucuu	CCAGAAAG
20	3293	ACUUUCUG	CUGAUGA	X	GAA	AAGACAGG	CCUGUCUUC	CAGAAAGU
	3306	UCCCGAUG	CUGAUGA	X	GAA	AUGCACUU	AAGUGCAUU	CAUCGGGA
	3307	GUCCCGAU	CUGAUGA	X	GAA	AAUGCACU	AGUGCAUUC	AUCGGGAC
	3310	CAGGUCCC	CUGAUGA	X	GAA	AUGAAUGC	GCAUUCAUC	GGGACCUG
	3333	GAUAAAAG	CUGAUGA	X	GAA	AUGUUUCU	AGAAACAUU	CUUUUAUC
25	3334	AGAUAAAA	CUGAUGA	X	GAA	AAUGUUUC	GAAACAUUC	UUUUAUCU
	3336	UCAGAUAA	CUGAUGA	X	GAA	AGAAUGUU	AACAUUCUU	UUAUCUGA
	3337	CUCAGAUA	CUGAUGA	X	GAA	AAGAAUGU	ACAUUCUUU	UAUCUGAG
	3338	UCUCAGAU	CUGAUGA	X	GAA	AAAGAAUG	CAUUCUUUU	AUCUGAGA
	3339	UUCUCAGA	CUGAUGA	X	GAA	AAAAGAAU	AUUCUUUUA	UCUGAGAA
30	3341	UGUUCUCA	CUGAUGA	X	GAA	AUAAAAGA	UCUUUUAUC	UGAGAACA
	3363	AAAUCACA	CUGAUGA	X	GAA	AUCUUCAC	GUGAAGAUU	UGUGAUUU
	3364	AAAAUCAC	CUGAUGA	X	GAA	AAUCUUCA	UGAAGAUUU	GUGAUUUU
	2270	אארריייאא	CHEATICA	v	CAA	אווראראאא	ITHIGHGAIRI	ITICCCOTT

	3371	CAAGGCCA	CUGAUGA	X	GAA	AAUCACAA	UUGUGAUUU	UGGCCUUG
	3372	GCAAGGCC	CUGAUGA	X	GAA	AAAUCACA	UGUGAUUUU	GGCCUUGC
	3378	UCCCGGGC	CUGAUGA	X	GAA	AGGCCAAA	UUUGGCCUU	GCCCGGGA
	3388	CUUAUAAA	CUGAUGA	X	GAA	AUCCCGGG	CCCGGGAUA	UUUAUAAG
5	3390	UUCUUAUA	CUGAUGA	X	GAA	AUAUCCCG	CGGGAUAUU	UAUAAGAA
	3391	GUUCUUAU	CUGAUGA	x	GAA	AAUAUCCC	GGGAUAUUU	AUAAGAAC
	3392	GGUUCUUA	CUGAUGA	X	GAA	AAAUAUCC	GGAUAUUUA	UAAGAACC
	3394	GGGGUUCU	CUGAUGA	X	GAA	AUAAAUAU	AUAUUUAUA	AGAACCCC
	3406	UCUCACAU	CUGAUGA	X	GAA	AUCGGGGU	ACCCCGAUU	AUGUGAGA
10	3407	UUCUCACA	CUGAUGA	X	GAA	AAUCGGGG	CCCCGAUUA	UGUGAGAA
	3424	AAGUCGAG	CUGAUGA	Х	GAA	AUCUCCUU	AAGGAGAUA	CUCGACUU
	3427	AGGAAGUC	CUGAUGA	X	GAA	AGUAUCUC	GAGAUACUC	GACUUCCU
	3432	UUCAGAGG	CUGAUGA	X	GAA	AGUCGAGU	ACUCGACUU	CCUCUGAA
	3433	UUUCAGAG	CUGAUGA	X	GAA	AAGUCGAG	CUCGACUUC	CUCUGAAA
15	3436	CCAUUUCA	CUGAUGA	X	GAA	AGGAAGUC	GACUUCCUC	UGAAAUGG
	3451	AGAUUCGG	CUGAUGA	X	GAA	AGCCAUCC	GGAUGGCUC	CCGAAUCU
	3458	CAAAGAUA	CUGAUGA	X	GAA	AUUCGGGA	UCCCGAAUC	UAUCUUUG
	3460	GUCAAAGA	CUGAUGA	X	GAA	AGAUUCGG	CCGAAUCUA	UCUUUGAC
	3462	UUGUCAAA	CUGAUGA	X	GAA	AUAGAUUC	GAAUCUAUC	UUUGACAA
20	3464	UUUUGUCA	CUGAUGA	X	GAA	AGAUAGAU	AUCUAUCUU	UGACAAAA
	3465	AUUUUGUC	CUGAUGA	X	GAA	AAGAUAGA	UCUAUCUUU	GACAAAAU
	3474	GUGCUGUA	CUGAUGA	X	GAA	AUUUUGUC	GACAAAAUC	UACAGCAC
	3476	UGGUGCUG	CUGAUGA	X	GAA	AGAUUUUG	CAAAAUCUA	CAGCACCA
	3500	CUCCGUAA	CUGAUGA	X	GAA	ACCACACG	CGUGUGGUC	UUACGGAG
2 5	3502	UACUCCGU	CUGAUGA	X	GAA	AGACCACA	UGUGGUCUU	ACGGAGUA
	3503	AUACUCCG	CUGAUGA	X	GAA	AAGACCAC	GUGGUCUUA	CGGAGUAU
	3510	CACAGCAA	CUGAUGA	X	GAA	ACUCCGUA	UACGGAGUA	UUGCUGUG
	3512	CCCACAGC	CUGAUGA	X	GAA	AUACUCCG	CGGAGUAUU	GCUGUGGG
	3525	AAGGAGAA	CUGAUGA	X	GAA	AUUUCCCA	UGGGAAAUC	UUCUCCUU
30	3527	CUAAGGAG	CUGAUGA	X	GAA	AGAUUUCC	GGAAAUCUU	CUCCUUAG
	3528	CCUAAGGA	CUGAUGA	X	GAA	AAGAUUUC	GAAAUCUUC	UCCUUAGG
	3530	CACCUAAG	CUGAUGA	X	GAA	AGAAGAUU	AAUCUUCUC	CUUAGGUG
	3533	ACCCACCU	CUGAUGA	X	GAA	AGGAGAAG	cuucuccuu	AGGUGGGU

PCT/US96/17480

WO 97/15662

	3534	GACCCACC	CUGAUGA	X	GAA	AAGGAGAA	UUCUCCUUA	GGUGGGUC
	3542	GGUAUGGA	CUGAUGA	X	GAA	ACCCACCU	AGGUGGGUC	UCCAUACC
	3544	UGGGUAUG	CUGAUGA	X	GAA	AGACCCAC	GUGGGUCUC	CAUACCCA
	3548	CUCCUGGG	CUGAUGA	X	GAA	AUGGAGAC	GUCUCCAUA	CCCAGGAG
5	3558	UCCAUUUG	CUGAUGA	X	GAA	ACUCCUGG	CCAGGAGUA	CAAAUGGA
	3575	GACUGCAA	CUGAUGA	X	GAA	AGUCCUCA	UGAGGACUU	UUGCAGUC
	3576	CGACUGCA	CUGAUGA	X	GAA	AAGUCCUC	GAGGACUUU	UGCAGUCG
	3577	GCGACUGC	CUGAUGA	X	GAA	AAAGUCCU	AGGACUUUU	GCAGUCGC
	3583	CCUCAGGC	CUGAUGA	X	GAA	ACUGCAAA	UUUGCAGUC	GCCUGAGG
10	3613	GUACUCAG	CUGAUGA	X	GAA	AGCUCUCA	UGAGAGCUC	CUGAGUAC
	3620	GAGUAGAG	CUGAUGA	X	GAA	ACUCAGGA	UCCUGAGUA	CUCUACUC
	3623	CAGGAGUA	CUGAUGA	X	GAA	AGUACUCA	UGAGUACUC	UACUCCUG
	3625	UUCAGGAG	CUGAUGA	X	GAA	AGAGUACU	AGUACUCUA	CUCCUGAA
	3628	GAUUUCAG	CUGAUGA	X	GAA	AGUAGAGU	ACUCUACUC	CUGAAAUC
15	3636	AUCUGAUA	CUGAUGA	X	GAA	AUUUCAGG	CCUGAAAUC	UAUCAGAU
	3638	UGAUCUGA	CUGAUGA	X	GAA	AGAUUUCA	UGAAAUCUA	UCAGAUCA
	3640	CAUGAUCU	CUGAUGA	X	GAA	AUAGAUUU	AAAUCUAUC	AGAUCAUG
	3645	UCCAGCAU	CUGAUGA	X	GAA	AUCUGAUA	UAUCAGAUC	AUGCUGGA
	3689	GUUCUGCA	CUGAUGA	X	GAA	AUCUUGGC	GCCAAGAUU	UGCAGAAC
20	3690	AGUUCUGC	CUGAUGA	X	GAA	AAUCUUGG	CCAAGAUUU	GCAGAACU
	3699	UUUUCCAC	CUGAUGA	X	GAA	AGUUCUGC	GCAGAACUU	GUGGAAAA
	3711	AAAUCACC	CUGAUGA	X	GAA	AGUUUUUC	GAAAAACUA	GGUGAUUU
	3718	UUGAAGCA	CUGAUGA	X	GAA	AUCACCUA	UAGGUGAUU	UGCUUCAA
	3719	CUUGAAGC	CUGAUGA	X	GAA	AAUCACCU	AGGUGAUUU	GCUUCAAG
25	3723	UUUGCUUG	CUGAUGA	X	GAA	AGCAAAUC	GAUUUGCUU	CAAGCAAA
	3724	AUUUGCUU	CUGAUGA	X	GAA	AAGCAAAU	AUUUGCUUC	AAGCAAAU
	3735	UCCUGUUG	CUGAUGA	X	GAA	ACAUUUGC	GCAAAUGUA	CAACAGGA
	3748	GUAGUCUU	CUGAUGA	X	GAA	ACCAUCCU	AGGAUGGUA	AAGACUAC
	3755	UUGGGAUG	CUGAUGA	X	GAA	AGUCUUUA	UAAAGACUA	CAUCCCAA
30	3759	UUGAUUGG	CUGAUGA	X	GAA	AUGUAGUC	GACUACAUC	CCAAUCAA
	3765	AUGGCAUU	CUGAUGA	X	GAA	AUUGGGAU	AUCCCAAUC	AAUGCCAU
	3774	CCUGUCAG	CUGAUGA	X	GAA	AUGGCAUU	AAUGCCAUA	CUGACAGG
	3787	AAACCCAC	CUGAUGA	X	GAA	AUUUCCUG	CAGGAAAUA	GUGGGUUU

	3794	AGUAUGUA	CUGAUGA	X	GAA	ACCCACUA	UAGUGGGUU	UACAUACU
	3795	GAGUAUGU	CUGAUGA	x	GAA	AACCCACU	AGUGGGUUU	ACAUACUC
	3796	UGAGUAUG	CUGAUGA	x	GAA	AAACCCAC	GUGGGUUUA	CAUACUCA
	3800	GAGUUGAG	CUGAUGA	x	GAA	AUGUAAAC	GUUUACAUA	CUCAACUC
5	3803	CAGGAGUU	CUGAUGA	x	GAA	AGUAUGUA	UACAUACUC	AACUCCUG
	3808	GAAGGCAG	CUGAUGA	X	GAA	AGUUGAGU	ACUCAACUC	CUGCCUUC
	3815	CCUCAGAG	CUGAUGA	X	GAA	AGGCAGGA	uccugccuu	CUCUGAGG
	3816	UCCUCAGA	CUGAUGA	x	GAA	AAGGCAGG	CCUGCCUUC	UCUGAGGA
	3818	AGUCCUCA	CUGAUGA	X	GAA	AGAAGGCA	UGCCUUCUC	UGAGGACU
10	3827	CCUUGAAG	CUGAUGA	X	GAA	AGUCCUCA	UGAGGACUU	CUUCAAGG
	3828	UCCUUGAA	CUGAUGA	X	GAA	AAGUCCUC	GAGGACUUC	UUCAAGGA
	3830	UUUCCUUG	CUGAUGA	X	GAA	AGAAGUCC	GGACUUCUU	CAAGGAAA
	3831	CUUUCCUU	CUGAUGA	X	GAA	AAGAAGUC	GACUUCUUC	AAGGAAAG
	3841	AGCUGAAA	CUGAUGA	X	GAA	ACUUUCCU	AGGAAAGUA	UUUCAGCU
15	3843	GGAGCUGA	CUGAUGA	x	GAA	AUACUUUC	GAAAGUAUU	UCAGCUCC
	3844	CGGAGCUG	CUGAUGA	x	GAA	AAUACUUU	AAAGUAUUU	CAGCUCCG
	3845	UCGGAGCU	CUGAUGA	X	GAA	AAAUACUU	AAGUAUUUC	AGCUCCGA
	3850	AAACUUCG	CUGAUGA	x	GAA	AGCUGAAA	UUUCAGCUC	CGAAGUUU
	3857	CUGAAUUA	CUGAUGA	X	GAA	ACUUCGGA	UCCGAAGUU	UAAUUCAG
20	3858	CCUGAAUU	CUGAUGA	X	GAA	AACUUCGG	CCGAAGUUU	AAUUCAGG
	3859	UCCUGAAU	CUGAUGA	x	GAA	AAACUUCG	CGAAGUUUA	AUUCAGGA
	3862	GCUUCCUG	CUGAUGA	X	GAA	AUUAAACU	AGUUUAAUU	CAGGAAGC
	3863	AGCUUCCU	CUGAUGA	X	GAA	AAUUAAAC	GUUUAAUUC	AGGAAGCU
	3872	CAUCAUCA	CUGAUGA	X	GAA	AGCUUCCU	AGGAAGCUC	UGAUGAUG
25	3882	ACAUAUCU	CUGAUGA	X	GAA	ACAUCAUC	GAUGAUGUC	AGAUAUGU
	3887	CAUUUACA	CUGAUGA	X	GAA	AUCUGACA	UGUCAGAUA	UGUAAAUG
	3891	AAAGCAUU	CUGAUGA	X	GAA	ACAUAUCU	AGAUAUGUA	AAUGCUUU
	3898	GAACUUGA	CUGAUGA	X	GAA	AGCAUUUA	UAAAUGCUU	UCAAGUUC
	3899	UGAACUUG	CUGAUGA	X	GAA	AAGCAUUU	AAAUGCUUU	CAAGUUCA
30	3900	AUGAACUU	CUGAUGA	X	GAA	AAAGCAUU	AAUGCUUUC	AAGUUCAU
	3905	GGCUCAUG	CUGAUGA	X	GAA	ACUUGAAA	UUUCAAGUU	CAUGAGCC
	3906	AGGCUCAU	CUGAUGA	X	GAA	AACUUGAA	UUCAAGUUC	AUGAGCCU
	3924	AAGGUUUU	CUGAUGA	X	GAA	AUUCUUUC	GAAAGAAUC	AAAACCUU

PCT/US96/17480

WO 97/15662

	3932	GUUCUUCA	CUGAUGA	X	GAA	AGGUUUUG	CAAAACCUU	UGAAGAAC
	3933	AGUUCUUC	CUGAUGA	X	GAA	AAGGUUUU	AAAACCUUU	GAAGAACU
	3942	UUCGGUAA	CUGAUGA	X	GAA	AGUUCUUC	GAAGAACUU	UUACCGAA
	3943	AUUCGGUA	CUGAUGA	X	GAA	AAGUUCUU	AAGAACUUU	UACCGAAU
5	3944	CAUUCGGU	CUGAUGA	X	GAA	AAAGUUCU	AGAACUUUU	ACCGAAUG
	3945	GCAUUCGG	CUGAUGA	X	GAA	AAAAGUUC	GAACUUUUA	CCGAAUGC
	3959	CAAACAUG	CUGAUGA	x	GAA	AGGUGGCA	UGCCACCUC	CAUGUUUG
	3965	AGUCAUCA	CUGAUGA	X	GAA	ACAUGGAG	CUCCAUGUU	UGAUGACU
	3966	UAGUCAUC	CUGAUGA	X	GAA	AACAUGGA	UCCAUGUUU	GAUGACUA
10	3974	CGCCCUGG	CUGAUGA	X	GAA	AGUCAUCA	UGAUGACUA	CCAGGGCG
	3994	GGCCAACA	CUGAUGA	X	GAA	AGUGCUGC	GCAGCACUC	UGUUGGCC
	3998	GAGAGGCC	CUGAUGA	X	GAA	ACAGAGUG	CACUCUGUU	GGCCUCUC
	4004	GCAUGGGA	CUGAUGA	X	GAA	AGGCCAAC	GUUGGCCUC	UCCCAUGC
	4006	CAGCAUGG	CUGAUGA	X	GAA	AGAGGCCA	UGGCCUCUC	CCAUGCUG
15	4022	UCCAGGUG	CUGAUGA	X	GAA	AGCGCUUC	GAAGCGCUU	CACCUGGA
	4023	GUCCAGGU	CUGAUGA	X	GAA	AAGCGCUU	AAGCGCUUC	ACCUGGAC
	4052	UCUUGAGC	CUGAUGA	X	GAA	AGGCCUUG	CAAGGCCUC	GCUCAAGA
	4056	UCAAUCUU	CUGAUGA	X	GAA	AGCGAGGC	GCCUCGCUC	AAGAUUGA
	4062	CUCAAGUC	CUGAUGA	X	GAA	AUCUUGAG	CUCAAGAUU	GACUUGAG
20	4067	UUACUCUC	CUGAUGA	X	GAA	AGUCAAUC	GAUUGACUU	GAGAGUAA
	4074	UUACUGGU	CUGAUGA	X	GAA	ACUCUCAA	UUGAGAGUA	ACCAGUAA
	4081	CUUACUUU	CUGAUGA	X	GAA	ACUGGUUA	UAACCAGUA	AAAGUAAG
	4087	CGACUCCU	CUGAUGA	X	GAA	ACUUUUAC	GUAAAAGUA	AGGAGUCG
	4094	ACAGCCCC	CUGAUGA	X	GAA	ACUCCUUA	UAAGGAGUC	GGGGCUGU
25	4103	UGACAUCA	CUGAUGA	X	GAA	ACAGCCCC	GGGGCUGUC	UGAUGUCA
	4110	GGCCUGCU	CUGAUGA	X	GAA	ACAUCAGA	UCUGAUGUC	AGCAGGCC
	4123	AUGGCAGA	CUGAUGA	X	GAA	ACUGGGCC	GGCCCAGUU	UCUGCCAU
	4124	AAUGGCAG	CUGAUGA	X	GAA	AACUGGGC	GCCCAGUUU	CUGCCAUU
	4125	GAAUGGCA	CUGAUGA	X	GAA	AAACUGGG	CCCAGUUUC	UGCCAUUC
30	4132	ACAGCUGG	CUGAUGA	. X	GAA	AUGGCAGA	UCUGCCAUU	CCAGCUGU
	4133	CACAGCUG	CUGAUGA	. X	GAA	AAUGGCAG	CUGCCAUUC	CAGCUGUG
	4149	ccuucgcu	CUGAUGA	. х	GAA	ACGUGCCC	GGGCACGUC	AGCGAAGG
	4169	CGUAGGUG	CUGAUGA	. X	GAA	ACCUGCGC	GCGCAGGUU	CACCUACG

	4170	UCGUAGGU	CUGAUGA	x	GAA	AACCUGCG	CGCAGGUUC	ACCUACGA
	4175	CGUGGUCG	CUGAUGA	x	GAA	AGGUGAAC	GUUCACCUA	CGACCACG
	4203	CAGCACGC	CUGAUGA	X	GAA	AUUUUCCU	AGGAAAAUC	GCGUGCUG
•	4214	GGGGCGGG	CUGAUGA	x	GAA	AGCAGCAC	GUGCUGCUC	CCCGCCCC
5	4229	CCGAGUUG	CUGAUGA	x	GAA	AGUCUGGG	CCCAGACUA	CAACUCGG
	4235	GGACCACC	CUGAUGA	x	GAA	AGUUGUAG	CUACAACUC	GGUGGUCC
	4242	GAGUACAG	CUGAUGA	X	GAA	ACCACCGA	UCGGUGGUC	CUGUACUC
	4247	GGGUGGAG	CUGAUGA	x	GAA	ACAGGACC	GGUCCUGUA	CUCCACCC
	4250	GUGGGGUG	CUGAUGA	X	GAA	AGUACAGG	CCUGUACUC	CACCCCAC
10	4263	AAACUCUA	CUGAUGA	x	GAA	AUGGGUGG	CCACCCAUC	UAGAGUUU
	4265	UCAAACUC	CUGAUGA	X	GAA	AGAUGGGU	ACCCAUCUA	GAGUUUGA
	4270	UCGUGUCA	CUGAUGA	X	GAA	ACUCUAGA	UCUAGAGUU	UGACACGA
	4271	UUCGUGUC	CUGAUGA	X	GAA	AACUCUAG	CUAGAGUUU	GACACGAA
	4284	CUAGAAAU	CUGAUGA	X	GAA	AGGCUUCG	CGAAGCCUU	AUUUCUAG
15	4285	UCUAGAAA	CUGAUGA	X	GAA	AAGGCUUC	GAAGCCUUA	UUUCUAGA
	4287	CUUCUAGA	CUGAUGA	X	GAA	AUAAGGCU	AGCCUUAUU	UCUAGAAG
	4288	GCUUCUAG	CUGAUGA	X	GAA	AAUAAGGC	GCCUUAUUU	CUAGAAGC
	4289	UGCUUCUA	CUGAUGA	X	GAA	AAAUAAGG	CCUUAUUUC	UAGAAGCA
	4291	UGUGCUUC	CUGAUGA	X	GAA	AGAAAUAA	UUAUUUCUA	GAAGCACA
20	4305	GGUAUAAA	CUGAUGA	X	GAA	ACACAUGU	ACAUGUGUA	UUUAUACC
	4307	GGGGUAUA	CUGAUGA	X	GAA	AUACACAU	AUGUGUAUU	UAUACCCC
	4308	GGGGGUAU	CUGAUGA	X	GAA	AAUACACA	UGUGUAUUU	AUACCCCC
	4309	UGGGGGUA	CUGAUGA	X	GAA	AAAUACAC	GUGUAUUUA	UACCCCCA
	4311	CCUGGGGG	CUGAUGA	X	GAA	AUAAAUAC	GUAUUUAUA	CCCCCAGG
25	4325	GCAAAAGC	CUGAUGA	X	GAA	AGUUUCCU	AGGAAACUA	GCUUUUGC
	4329	ACUGGCAA	CUGAUGA	X	GAA	AGCUAGUU	AACUAGCUU	UUGCCAGU
	4330	UACUGGCA	CUGAUGA	X	GAA	AAGCUAGU	ACUAGCUUU	UGCCAGUA
	4331	AUACUGGC	CUGAUGA	X	GAA	AAAGCUAG	CUAGCUUUU	GCCAGUAU
	4338	AUGCAUAA	CUGAUGA	X	GAA	ACUGGCAA	UUGCCAGUA	UUAUGCAU
30	4340	AUAUGCAU	CUGAUGA	X	GAA	AUACUGGC	GCCAGUAUU	AUGCAUAU
	4341	UAUAUGCA	CUGAUGA	X	GAA	AAUACUGG	CCAGUAUUA	UGCAUAUA
	4347	AACUUAUA	CUGAUGA	X	GAA	AUGCAUAA	UUAUGCAUA	UAUAAGUU
	4349	UAAACUUA	CUGAUGA	X	GAA	AUAUGCAU	AUGCAUAUA	UAAGUUUA

	4351	UGUAAACU	CUGAUGA	X	GAA	AUAUAUGC	GCAUAUAUA	AGUUUACA
	4355	AAGGUGUA	CUGAUGA	X	GAA	ACUUAUAU	AUAUAAGUU	UACACCUU
	4356	AAAGGUGU	CUGAUGA	X	GAA	AACUUAUA	UAUAAGUUU	ACACCUUU
	4357	UAAAGGUG	CUGAUGA	X	GAA	AAACUUAU	AUAAGUUUA	CACCUUUA
5	4363	GAAAGAUA	CUGAUGA	X	GAA	AGGUGUAA	UUACACCUU	UAUCUUUC
	4364	GGAAAGAU	CUGAUGA	X	GAA	AAGGUGUA	UACACCUUU	AUCUUUCC
	4365	UGGAAAGA	CUGAUGA	X	GAA	AAAGGUGU	ACACCUUUA	UCUUUCCA
	4367	CAUGGAAA	CUGAUGA	X	GAA	AUAAAGGU	ACCUUUAUC	UUUCCAUG
	4369	CCCAUGGA	CUGAUGA	X	GAA	AGAUAAAG	CUUUAUCUU	UCCAUGGG
10	4370	UCCCAUGG	CUGAUGA	X	GAA	AAGAUAAA	UUUAUCUUU	CCAUGGGA
	4371	CUCCCAUG	CUGAUGA	X	GAA	AAAGAUAA	UUAUCUUUC	CAUGGGAG
	4389	AUCACAAA	CUGAUGA	X	GAA	AGCAGCUG	CAGCUGCUU	UUUGUGAU
	4390	AAUCACAA	CUGAUGA	X	GAA	AAGCAGCU	AGCUGCUUU	UUGUGAUU
	4391	AAAUCACA	CUGAUGA	X	GAA	AAAGCAGC	GCUGCUUUU	UGUGAUUU
15	4392	AAAAUCAC	CUGAUGA	X	GAA	AAAAGCAG	CUGCUUUUU	GUGAUUUU
	4398	AAAAAUUA	CUGAUGA	X	GAA	AUCACAAA	UUUGUGAUU	UAAUUUUU
	4399	UAUUAAAA	CUGAUGA	X	GAA	AAUCACAA	UUGUGAUUU	AUAAUUU
	4400	CUAUUAAA	CUGAUGA	X	GAA	AAAUCACA	UGUGAUUUU	UUUAAUAG
	4401	ACUAUUAA	CUGAUGA	X	GAA	AAAAUCAC	GUGAUUUUU	UUAAUAGU
20	4402	CACUAUUA	CUGAUGA	X	GAA	AAAAAUCA	UGAUUUUUU	UAAUAGUG
	4403	GCACUAUU	CUGAUGA	X	GAA	AAAAAAUC	GAUUUUUUU	AAUAGUGC
	4404	AGCACUAU	CUGAUGA	X	GAA	UAAAAAA	AUUUUUUUA	AUAGUGCU
	4407	AAAAGCAC	CUGAUGA	X	GAA	AUUAAAAA	UUUUUAAUA	GUGCUUUU
	4413	AAAAAAA	CUGAUGA	X	GAA	AGCACUAU	AUAGUGCUU	טטטטטטטט
25	4414	AAAAAAA	CUGAUGA	X	GAA	AAGCACUA	UAGUGCUUU	טטטטטטטט
	4415	САААААА	CUGAUGA	X	GAA	AAAGCACU	AGUGCUUUU	บบบบบบบ
	4416	UCAAAAA	CUGAUGA	X	GAA	AAAAGCAC	GUGCUUUUU	UUUUUUGA
	4417	GUCAAAAA	CUGAUGA	X	GAA	AAAAAGCA	ugcuuuuuu	UUUUUGAC
	4418	AGUCAAAA	CUGAUGA	X	GAA	AAAAAAGC	GCUUUUUUU	UUUUGACU
30	4419	UAGUCAAA	CUGAUGA	X	GAA	AAAAAAAG	cuuuuuuu	UUUGACUA
	4420	UUAGUCAA	CUGAUGA	X	GAA	AAAAAAA	טטטטטטטטט	UUGACUAA
	4421	GUUAGUCA	CUGAUGA	X	GAA	AAAAAA	บบบบบบบบบ	UGACUAAC
	4422	UGUUAGUC	CUGAUGA	X	GAA	AAAAAA	บบบบบบบบบ	GACUAACA

69

AUUCUUGU CUGAUGA X GAA AGUCAAAA UUUUGACUA ACAAGAAU 4427 4438 UCUGGAGU CUGAUGA X GAA ACAUUCUU AAGAAUGUA ACUCCAGA 4442 UCUAUCUG CUGAUGA X GAA AGUUACAU AUGUAACUC CAGAUAGA 4448 UAUUUCUC CUGAUGA X GAA AUCUGGAG CUCCAGAUA GAGAAAUA 4456 CUUGUCAC CUGAUGA X GAA AUUUCUCU AGAGAAAUA GUGACAAG 4476 UUUAGCAG CUGAUGA X GAA AGUGUUCU AGAACACUA CUGCUAAA 4482 UGAGGAUU CUGAUGA X GAA AGCAGUAG CUACUGCUA AAUCCUCA 4486 AACAUGAG CUGAUGA X GAA AUUUAGCA UGCUAAAUC CUCAUGUU 4489 AGUAACAU CUGAUGA X GAA AGGAUUUA UAAAUCCUC AUGUUACU 4494 CACUGAGU CUGAUGA X GAA ACAUGAGG CCUCAUGUU ACUCAGUG 10 4495 ACACUGAG CUGAUGA X GAA AACAUGAG CUCAUGUUA CUCAGUGU 4498 CUAACACU CUGAUGA X GAA AGUAACAU AUGUUACUC AGUGUUAG 4504 AUUUCUCU CUGAUGA X GAA ACACUGAG CUCAGUGUU AGAGAAAU 4505 GAUUUCUC CUGAUGA X GAA AACACUGA UCAGUGUUA GAGAAAUC 4513 UUAGGAAG CUGAUGA X GAA AUUUCUCU AGAGAAAUC CUUCCUAA 15 4516 GGULUAGG CUGAUGA X GAA AGGAUUUC GAAAUCCUU CCUAAACC GGGUUUAG CUGAUGA X GAA AAGGAUUU AAAUCCUUC CUAAACCC 4517 AUUGGGUU CUGAUGA X GAA AGGAAGGA UCCUUCCUA AACCCAAU 4520 GAGCAGGG CUGAUGA X GAA AGUCAUUG CAAUGACUU CCCUGCUC 4533 AAUGACUUC CCUGCUCC 20 4534 GGAGCAGG CUGAUGA X GAA AAGUCAUU 4541 GGGGGUUG CUGAUGA X GAA AGCAGGGA UCCCUGCUC CAACCCCC CGUGCCCU CUGAUGA X GAA AGGUGGCG CGCCACCUC AGGGCACG 4557 GGACCAGUU UGAUUGAG 4576 CUCAAUCA CUGAUGA X GAA ACUGGUCC GACCAGUUU GAUUGAGG 4577 CCUCAAUC CUGAUGA X GAA AACUGGUC 25 4581 AGCUCCUC CUGAUGA X GAA AUCAAACU AGUUUGAUU GAGGAGCU 4598 CAUUGGGU CUGAUGA X GAA AUCAGUGC GCACUGAUC ACCCAAUG 4610 GGGUACGU CUGAUGA X GAA AUGCAUUG CAAUGCAUC ACGUACCC CAGUGGGG CUGAUGA X GAA ACGUGAUG CAUCACGUA CCCCACUG 4615 CUGGGGCU CUGAUGA X GAA ACGGGCUU AAGCCCGUU AGCCCCAG 4664 4665 CCUGGGGC CUGAUGA X GAA AACGGGCU AGCCCGUUA GCCCCAGG 30 4678 CAGCCAGU CUGAUGA X GAA AUCCCCUG CAGGGGAUC ACUGGCUG 4700 ACUCCCGA CUGAUGA X GAA AUGUUGCU AGCAACAUC UCGGGAGU 4702 GGACUCCC CUGAUGA X GAA AGAUGUUG CAACAUCUC GGGAGUCC

	4709	UGCUAGAG	CUGAUGA	X	GAA	ACUCCCGA	UCGGGAGUC	CUCUAGCA
	4712	GCCUGCUA	CUGAUGA	X	GAA	AGGACUCC	GGAGUCCUC	UAGCAGGC
	4714	AGGCCUGC	CUGAUGA	X	GAA	AGAGGACU	AGUCCUCUA	GCAGGCCU
	4723	ACAUGUCU	CUGAUGA	X	GAA	AGGCCUGC	GCAGGCCUA	AGACAUGU
5	4802	GCGUCUCA	CUGAUGA	X	GAA	AUUCUUUC	GAAAGAAUU	UGAGACGC
	4803	UGCGUCUC	CUGAUGA	X	GAA	AAUUCUUU	AAAGAAUUU	GAGACGCA
	4840	GCAUUGCU	CUGAUGA	X	GAA	AGCCCCGU	ACGGGGCUC	AGCAAUGC
	4852	GCCACUGA	CUGAUGA	X	GAA	AUGGCAUU	AAUGCCAUU	UCAGUGGC
	4853	AGCCACUG	CUGAUGA	X	GAA	AAUGGCAU	AUGCCAUUU	CAGUGGCU
10	4854	AAGCCACU	CUGAUGA	X	GAA	AAAUGGCA	UGCCAUUUC	AGUGGCUU
	4862	GAGCUGGG	CUGAUGA	X	GAA	AGCCACUG	CAGUGGCUU	CCCAGCUC
	4863	AGAGCUGG	CUGAUGA	X	GAA	AAGCCACU	AGUGGCUUC	CCAGCUCU
	4870	AAGGGUCA	CUGAUGA	X	GAA	AGCUGGGA	UCCCAGCUC	UGACCCUU
	4878	AAAUGUAG	CUGAUGA	X	GAA	AGGGUCAG	CUGACCCUU	CUACAUUU
15	4879	CAAAUGUA	CUGAUGA	X	GAA	AAGGGUCA	UGACCCUUC	UACAUUUG
	4881	CUCAAAUG	CUGAUGA	X	GAA	AGAAGGGU	ACCCUUCUA	CAUUUGAG
	4885	GGCCCUCA	CUGAUGA	X	GAA	AUGUAGAA	UUCUACAUU	UGAGGCC
	4886	GGGCCCUC	CUGAUGA	X	GAA	AAUGUAGA	UCUACAUUU	GAGGGCCC
	4929	AUCCAGAA	CUGAUGA	X	GAA	AUGUCCCC	GGGGACAUU	UUCUGGAU
20	4930	AAUCCAGA	CUGAUGA	X	GAA	AAUGUCCC	GGGACAUUU	UCUGGAUU
	4931	GAAUCCAG	CUGAUGA	X	GAA	AAAUGUCC	GGACAUUUU	CUGGAUUC
	4932	AGAAUCCA	CUGAUGA	X	GAA	AAAAUGUC	GACAUUUUC	UGGAUUCU
	4938	CCUCCCAG	CUGAUGA	X	GAA	AUCCAGAA	UUCUGGAUU	CUGGGAGG
	4939	GCCUCCCA	CUGAUGA	X	GAA	AAUCCAGA	UCUGGAUUC	UGGGAGGC
25	4963	AAAAAAGA	CUGAUGA	X	GAA	AUUUGUCC	GGACAAAUA	טכטטטטטט
	4965	CCAAAAAA	CUGAUGA	X	GAA	AUAUUUGU	ACAAAUAUC	UUUUUUGG
	4967	UUCCAAAA	CUGAUGA	X	GAA	AGAUAUUU	AAAUAUCUU	UUUUGGAA
	4968	GUUCCAAA	CUGAUGA	X	GAA	AAGAUAUU	AAUAUCUUU	UUUGGAAC
	4969	AGUUCCAA	CUGAUGA	X	GAA	AAAGAUAU	AUAUCUUUU	UUGGAACU
30	4970	UAGUUCCA	CUGAUGA	X	GAA	AAAAGAUA	UAUCUUUUU	UGGAACUA
	4971	UUAGUUCC	CUGAUGA	X	GAA	AAAAAGAU	AUCUUUUUU	GGAACUAA
	4978	AUUUGCUU	CUGAUGA	X	GAA	AGUUCCAA	UUGGAACUA	AAGCAAAU
	4987	AGGUCUAA	CUGAUGA	X	GAA	AUUUGCUU	AAGCAAAUU	UUAGACCU

	4988	AAGGUCUA	CUGAUGA	X	GAA	AAUUUGCU	AGCAAAUUU	UAGACCUU
	4989	AAAGGUCU	CUGAUGA	X	GAA	AAAUUUGC	GCAAAUUUU	AGACCUUU
	49 90	UAAAGGUC	CUGAUGA	X	GAA	AAAAUUUG	CAAAUUUUA	GACCUUUA
	4996	CAUAGGUA	CUGAUGA	X	GAA	AGGUCUAA	UUAGACCUU	UACCUAUG
5	4997	CCAUAGGU	CUGAUGA	X	GAA	AAGGUCUA	UAGACCUUU	ACCUAUGG
	4998	UCCAUAGG	CUGAUGA	X	GAA	AAAGGUCU	AGACCUUUA	CCUAUGGA
	5002	CACUUCCA	CUGAUGA	X	GAA	AGGUAAAG	CUUUACCUA	UGGAAGUG
	5013	GGACAUAG	CUGAUGA	X	GAA	ACCACUUC	GAAGUGGUU	CUAUGUCC
	5014	UGGACAUA	CUGAUGA	x	GAA	AACCACUU	AAGUGGUUC	UAUGUCCA
10	5016	AAUGGACA	CUGAUGA	X	GAA	AGAACCAC	GUGGUUCUA	UGUCCAUU
	5020	UGAGAAUG	CUGAUGA	X	GAA	ACAUAGAA	UUCUAUGUC	CAUUCUCA
	5024	CGAAUGAG	CUGAUGA	X	GAA	AUGGACAU	AUGUCCAUU	CUCAUUCG
	5025	ACGAAUGA	CUGAUGA	X	GAA	AAUGGACA	UGUCCAUUC	UCAUUCGU
	5027	CCACGAAU	CUGAUGA	X	GAA	AGAAUGGA	UCCAUUCUC	AUUCGUGG
15	503 0	AUGCCACG	CUGAUGA	Х	GAA	AUGAGAAU	AUUCUCAUU	CGUGGCAU
	5031	CAUGCCAC	CUGAUGA	X	GAA	AAUGAGAA	UUCUCAUUC	GUGGCAUG
	5041	CAAAUCAA	CUGAUGA	X	GAA	ACAUGCCA	UGGCAUGUU	UUGAUUUG
	5042	ACAAAUCA	CUGAUGA	X	GAA	AACAUGCĊ	GGCAUGUUU	UGAUUUGU
	5043	UACAAAUC	CUGAUGA	X	GAA	AAACAUGC	GCAUGUUUU	GAUUUGUA
20	5047	GUGCUACA	CUGAUGA	X	GAA	AUCAAAAC	GUUUUGAUU	UGUAGCAC
	5048	AGUGCUAC	CUGAUGA	X	GAA	AAUCAAAA	UUUUGAUUU	GUAGCACU
	5051	CUCAGUGC	CUGAUGA	X	GAA	ACAAAUCA	UGAUUUGUA	GCACUGAG
	5069	UCAGAGUU	CUGAUGA	X	GAA	AGUGCCAC	GUGGCACUC	AACUCUGA
	5074	UGGGCUCA	CUGAUGA	X	GAA	AGUUGAGU	ACUCAACUC	UGAGCCCA
25	5084	GCCAAAAG	CUGAUGA	X	GAA	AUGGGCUC	GAGCCCAUA	CUUUUGGC
	5087	GGAGCCAA	CUGAUGA	X	GAA	AGUAUGGG	CCCAUACUU	UUGGCUCC
	5088	AGGAGCCA	CUGAUGA	X	GAA	AAGUAUGG	CCAUACUUU	UGGCUCCU
	508 9	GAGGAGCC	CUGAUGA	X	GAA	AAAGUAUG	CAUACUUUU	GGCUCCUC
	5094	UACUAGAG	CUGAUGA	X	GAA	AGCCAAAA	UUUUGGCUC	CUCUAGUA
30	5097	UCUUACUA	CUGAUGA	X	GAA	AGGAGCCA	UGGCUCCUC	UAGUAAGA
	5099	CAUCUUAC	CUGAUGA	X	GAA	AGAGGAGC	GCUCCUCUA	GUAAGAUG
	5102	GUGCAUCU	CUGAUGA	X	GAA	ACUAGAGG	CCUCUAGUA	AGAUGCAC
	5119	CUCUGGCU	CUGAUGA	x	GAA	AGUUUUCA	UGAAAACUU	AGCCAGAG

72

WO 97/15662

	5120	ACUCUGGC	CUGAUGA	Х	GAA	AAGUUUUC	GAAAACUUA	GCCAGAGU
	5129	GACAACCU	CUGAUGA	X	GAA	ACUCUGGC	GCCAGAGUU	AGGUUGUC
	5130	AGACAACC	CUGAUGA	X	GAA	AACUCUGG	CCAGAGUUA	GGUUGUCU
	5134	CUGGAGAC	CUGAUGA	X	GAA	ACCUAACU	AGUUAGGUU	GUCUCCAG
5	5137	GGCCUGGA	CUGAUGA	X	GAA	ACAACCUA	UAGGUUGUC	UCCAGGCC
	5139	AUGGCCUG	CUGAUGA	X	GAA	AGACAACC	GGUUGUCUC	CAGGCCAU
	5156	UUCAGUGU	CUGAUGA	X	GAA	AGGCCAUC	GAUGGCCUU	ACACUGAA
	5157	UUUCAGUG	CUGAUGA	X	GAA	AAGGCCAU	AUGGCCUUA	CACUGAAA
	5170	UAGAAUGU	CUGAUGA	X	GAA	ACAUUUUC	GAAAAUGUC	ACAUUCUA
10	5175	CAAAAUAG	CUGAUGA	X	GAA	AUGUGACA	UGUCACAUU	CUAUUUUG
	5176	CCAAAAUA	CUGAUGA	X	GAA	AAUGUGAC	GUCACAUUC	UAUUUUGG
	5178	ACCCAAAA	CUGAUGA	X	GAA	AGAAUGUG	CACAUUCUA	UUUUGGGU
	5180	AUACCCAA	CUGAUGA	X	GAA	AUAGAAUG	CAUUCUAUU	UUGGGUAU
	5181	AAUACCCA	CUGAUGA	X	GAA	AAUAGAAU	AUUCUAUUU	UGGGUAUU
15	5182	UAAUACCC	CUGAUGA	X	GAA	AAAUAGAA	UUCUAUUUU	GGGUAUUA
	5187	AAUUAUAA	CUGAUGA	X	GAA	ACCCAAAA	UUUUGGGUA	UUAAUAUA
	5189	UUAUAUAU	CUGAUGA	X	GAA	AUACCCAA	UUGGGUAUU	AAUAUAUA
	5190	CUAUAUAU	CUGAUGA	X	GAA	AAUACCCA	UGGGUAUUA	AUAUAUAG
	5193	GGACUAUA	CUGAUGA	X	GAA	AUUAAUAC	GUAUUAAUA	UAUAGUCC
20	5195	CUGGACUA	CUGAUGA	X	GAA	AUAUUAAU	AUUAAUAUA	UAGUCCAG
	5197	GUCUGGAC	CUGAUGA	X	GAA	AUAUAUUA	UAAUAUAUA	GUCCAGAC
	5200	AGUGUCUG	CUGAUGA	X	GAA	ACUAUAUA	UAUAUAGUC	CAGACACU
	5209	AUUGAGUU	CUGAUGA	X	GAA	AGUGUCUG	CAGACACUU	AACUCAAU
	5210	AAUUGAGU	CUGAUGA	X	GAA	AAGUGUCU	AGACACUUA	ACUCAAUU
25	5214	AAGAAAUU	CUGAUGA	X	GAA	AGUUAAGU	ACUUAACUC	AAUUUCUU
	5218	UACCAAGA	CUGAUGA	X	GAA	AUUGAGUU	AACUCAAUU	UCUUGGUA
	5219	AUACCAAG	CUGAUGA	X	GAA	AAUUGAGU	ACUCAAUUU	CUUGGUAU
	5220	AAUACCAA	CUGAUGA	X	GAA	AAAUUGAG	CUCAAUUUC	UUGGUAUU
	5222	AUAAUACC	CUGAUGA	X	GAA	AGAAAUUG	CAAUUUCUU	GGUAUUAU
30	5226	CAGAAUAA	CUGAUGA	X	GAA	ACCAAGAA	UUCUUGGUA	UUAUUCUG
	5228	AACAGAAU	CUGAUGA	X	GAA	AUACCAAG	CUUGGUAUU	AUUCUGUU
	5229	AAACAGAA	CUGAUGA	X	GAA	AAUACCAA	UUGGUAUUA	บบดบบบบ
	5231	CAAAACAG	CUGAUGA	X	GAA	AUAAUACC	GGUAUUAUU	CUGUUUUUG

	5232	GCAAAACA	CUGAUGA	X	GAA	AAUAAUAC	GUAUUAUUC	UGUUUUGC
	5236	CUGUGCAA	CUGAUGA	X	GAA	ACAGAAUA	UAUUCUGUU	UUGCACAG
	5237	ACUGUGCA	CUGAUGA	X	GAA	AACAGAAU	AUUCUGUUU	UGCACAGU
	5238	AACUGUGC	CUGAUGA	X	GAA	AAACAGAA	UUCUGUUUU	GCACAGUU
5	5246	UCACAACU	CUGAUGA	X	GAA	ACUGUGCA	UGCACAGUU	AGUUGUGA
	5247	UUCACAAC	CUGAUGA	X	GAA	AACUGUGC	GCACAGUUA	GUUGUGAA
	5250	UCUUUCAC	CUGAUGA	X	GAA	ACUAACUG	CAGUUAGUU	GUGAAAGA
	5284	CUCCUCAG	CUGAUGA	X	GAA	ACUGCAUU	AAUGCAGUC	CUGAGGAG
	5296	AUGGAGAA	CUGAUGA	X	GAA	ACUCUCCU	AGGAGAGUU	UUCUCCAU
10	5297	UAUGGAGA	CUGAUGA	X	GAA	AACUCUCC	GGAGAGUUU	UCUCCAUA
	5298	AUAUGGAG	CUGAUGA	X	GAA	AAACUCUC	GAGAGUUUU	CUCCAUAU
	5299	GAUAUGGA	CUGAUGA	X	GAA	AAAACUCU	AGAGUUUUC	UCCAUAUC
	5301	UUGAUAUG	CUGAUGA	X	GAA	AGAAAACU	AGUUUUCUC	CAUAUCAA
	5305	CGUUUUGA	CUGAUGA	X	GAA	AUGGAGAA	UUCUCCAUA	UCAAAACG
15	5307	CUCGUUUU	CUGAUGA	X	GAA	AUAUGGAG	CUCCAUAUC	AAAAC GA G
	5336	ACCUUAUU	CUGAUGA	X	GAA	ACCUUUUU	AAAAAGGUC	AAUAAGGU
	534 0	CUUGACCU	CUGAUGA	X	GAA	AUUGACCU	AGGUCAAUA	AGGUCAAG
	5345	CUUCCCUU	CUGAUGA	X	GAA	ACCUUAUU	AAUAAGGUC	AAGGGAAG
	5361	GGUAUAGA	CUGAUGA	X	GAA	ACGGGGUC	GACCCCGUC	UCUAUACC
20	5363	UUGGUAUA	CUGAUGA	X	GAA	AGACGGGG	ccccgucuc	UAUACCAA
	5365	GGUUGGUA	CUGAUGA	X	GAA	AGAGACGG	CCGUCUCUA	UACCAACC
	5367	UUGGUUGG	CUGAUGA	X	GAA	AUAGAGAC	GUCUCUAUA	CCAACCAA
	5382	UGUUGGUG	CUGAUGA	X	GAA	AUUGGUUU	AAACCAAUU	CACCAACA
	5383	GUGUUGGU	CUGAUGA	X	GAA	AAUUGGUU	AACCAAUUC	ACCAACAC
25	5395	UGGGUCCC	CUGAUGA	X	GAA	ACUGUGUU	AACACAGUU	GGGACCCA
	5417	ACGUGACU	CUGAUGA	X	GAA	ACUUCCUG	CAGGAAGUC	AGUCACGU
	5421	GGAAACGU	CUGAUGA	X	GAA	ACUGACUU	AAGUCAGUC	ACGUUUCC
	5426	GAAAAGGA	CUGAUGA	X	GAA	ACGUGACU	AGUCACGUU	uccuuuuc
	5427	UGAAAAGG	CUGAUGA	X	GAA	AACGUGAC	GUCACGUUU	CCUUUUCA
30	5428	AUGAAAAG	CUGAUGA	X	GAA	AAACGUGA	UCACGUUUC	CUUUUCAU
	5431	UAAAUGAA	CUGAUGA	X	GAA	AGGAAACG	CGUUUCCUU	UUCAUUUA
	5432	UUAAAUGA	CUGAUGA	X	GAA	AAGGAAAC	GUUUCCUUU	UCAUUUAA
	5433	AUUAAAUG	CUGAUGA	X	GAA	AAAGGAAA	ນບຸນດວດກຸກກຸ	CAUUUAAU

	5434	CAUUAAAU	CUGAUGA	X	GAA	AAAAGGAA	UUCCUUUUC	AUUUAAUG
	5437	CCCCAUUA	CUGAUGA	X	GAA	AUGAAAAG	CUUUUCAUU	UAAUGGGG
	5438	UCCCCAUU	CUGAUGA	X	GAA	AAUGAAAA	UUUUCAUUU	AAUGGGGA
	5439	AUCCCCAU	CUGAUGA	X	GAA	AAAUGAAA	UUUCAUUUA	AUGGGGAU
5	5448	GAUAGUGG	CUGAUGA	X	GAA	AUCCCCAU	AUGGGGAUU	CCACUAUC
	5449	AGAUAGUG	CUGAUGA	X	GAA	AAUCCCCA	UGGGGAUUC	CACUAUCU
	5454	GUGUGAGA	CUGAUGA	X	GAA	AGUGGAAU	AUUCCACUA	UCUCACAC
	5456	UAGUGUGA	CUGAUGA	X	GAA	AUAGUGGA	UCCACUAUC	UCACACUA
	5458	AUUAGUGU	CUGAUGA	X	GAA	AGAUAGUG	CACUAUCUC	ACACUAAU
LO	5464	UUUCAGAU	CUGAUGA	X	GAA	AGUGUGAG	CUCACACUA	AUCUGAAA
	5467	UCCUUUCA	CUGAUGA	X	GAA	AUUAGUGU	ACACUAAUC	UGAAAGGA
	5489	CGCCAGCU	CUGAUGA	X	GAA	AUGCUCUU	AAGAGCAUU	AGCUGGCG
	5490	GCGCCAGC	CUGAUGA	X	GAA	AAUGCUCU	AGAGCAUUA	GCUGGCGC
	5501	GUGCUUAA	CUGAUGA	X	GAA	AUGCGCCA	UGGCGCAUA	UUAAGCAC
15	5503	AAGUGCUU	CUGAUGA	X	GAA	AUAUGCGC	GCGCAUAUU	AAGCACUU
	5504	AAAGUGCU	CUGAUGA	X	GAA	AAUAUGCG	CGCAUAUUA	AGCACUUU
	5511	GGAGCUUA	CUGAUGA	X	GAA	AGUGCUUA	UAAGCACUU	UAAGCUCC
	5512	AGGAGCUU	CUGAUGA	X	GAA	AAGUGCUU	AAGCACUUU	AAGCUCCU
	5513	AAGGAGCU	CUGAUGA	X	GAA	AAAGUGCU	AGCACUUUA	AGCUCCUU
20	5518	UACUCAAG	CUGAUGA	X	GAA	AGCUUAAA	UUUAAGCUC	CUUGAGUA
	5521	UUUUACUC	CUGAUGA	X	GAA	AGGAGCUU	AAGCUCCUU	GAGUAAAA
	5526	CACCUUUU	CUGAUGA	X	GAA	ACUCAAGG	CCUUGAGUA	AAAAGGUG
	5537	AAAUUACA	CUGAUGA	X	GAA	ACCACCUU	AAGGUGGUA	UGUAAUUU
	5541	GCAUAAAU	CUGAUGA	X	GAA	ACAUACCA	UGGUAUGUA	AUUUAUGC
25	5544	CUUGCAUA	CUGAUGA	X	GAA	AUUACAUA	UAUGUAAUU	UAUGCAAG
	554 5	CCUUGCAU	CUGAUGA	X	GAA	AAUUACAU	AUGUAAUUU	AUGCAAGG
	5546	ACCUUGCA	CUGAUGA	X	GAA	AAAUUACA	UGUAAUUUA	UGCAAGGU
	55 55	UGGAGAAA	CUGAUGA	X	GAA	ACCUUGCA	UGCAAGGUA	UUUCUCCA
	5557	ACUGGAGA	CUGAUGA	X	GAA	AUACCUUG	CAAGGUAUU	UCUCCAGU
30	5558	AACUGGAG	CUGAUGA	X	GAA	AAUACCUU	AAGGUAUUU	CUCCAGUU
	5 5 59	CAACUGGA	CUGAUGA	X	GAA	AAAUACCU	AGGUAUUUC	UCCAGUUG
	5561	CCCAACUG	CUGAUGA	X	GAA	AGAAAUAC	GUAUUUCUC	CAGUUGGG
	5566	UGAGUCCC	CUGAUGA	X	GAA	ACUGGAGA	UCUCCAGUU	GGGACUCA

	5573	AAUAUCCU	CUGAUGA	x	GAA	AGUCCCAA	UUGGGACUC	AGGAUAUU
	5579	UUAACUAA	CUGAUGA	X	GAA	AUCCUGAG	CUCAGGAUA	UUAGUUAA
	5581	CAUUAACU	CUGAUGA	X	GAA	AUAUCCUG	CAGGAUAUU	AGUUAAUG
	5582	UCAUUAAC	CUGAUGA	X	GAA	AAUAUCCU	AGGAUAUUA	GUUAAUGA
5	5585	GGCUCAUU	CUGAUGA	X	GAA	ACUAAUAU	AUAUUAGUU	AAUGAGCC
	5586	UGGCUCAU	CUGAUGA	X	GAA	AACUAAUA	UAUUAGUUA	AUGAGCCA
	5596	CUUCUAGU	CUGAUGA	X	GAA	AUGGCUCA	UGAGCCAUC	ACUAGAAG
	5600	υυυυςυυς	CUGAUGA	X	GAA	AGUGAUGG	CCAUCACUA	GAAGAAAA
	5615	CAGUUGAA	CUGAUGA	X	GAA	AUGGGCUU	AAGCCCAUU	UUCAACUG
10	5616	GCAGUUGA	CUGAUGA	X	GAA	AAUGGGCU	AGCCCAUUU	UCAACUGC
	5617	AGCAGUUG	CUGAUGA	X	GAA	AAAUGGGC	GCCCAUUUU	CAACUGCU
	5618	AAGCAGUU	CUGAUGA	X	GAA	AAAAUGGG	CCCAUUUUC	AACUGCUU
	5626	AAGUUUCA	CUGAUGA	X	GAA	AGCAGUUG	CAACUGCUU	UGAAACUU
	5627	CAAGUUUC	CUGAUGA	X	GAA	AAGCAGUU	AACUGCUUU	GAAACUUG
15	5634	CCCCAGGC	CUGAUGA	X	GAA	AGUUUCAA	UUGAAACUU	GCCUGGGG
	5644	CAUGCUCA	CUGAUGA	X	GAA	ACCCCAGG	CCUGGGGUC	UGAGCAUG
	5661	UGUCUCCC	CUGAUGA	X	GAA	AUUCCCAU	AUGGGAAUA	GGGAGACA
	5674	CCCUUUCC	CUGAUGA	X	GAA	ACCCUGUC	GACAGGGUA	GGAAAGGG
	5688	CUGAAGAG	CUGAUGA	X	GAA	AGGCGCCC	GGGCGCCUA	CUCUUCAG
20	5691	ACCCUGAA	CUGAUGA	X	GAA	AGUAGGCG	CGCCUACUC	UUCAGGGU
	5693	AGACCCUG	CUGAUGA	X	GAA	AGAGUAGG	CCUACUCUU	CAGGGUCU
	5694	UAGACCCU	CUGAUGA	X	GAA	AAGAGUAG	CUACUCUUC	AGGGUCUA
	57 00	GAUCUUUA	CUGAUGA	X	GAA	ACCCUGAA	UUCAGGGUC	UAAAGAUC
	5702	UUGAUCUU	CUGAUGA	X	GAA	AGACCCUG	CAGGGUCUA	AAGAUCAA
25	5708	GCCCACUU	CUGAUGA	X	GAA	AUCUUUAG	CUAAAGAUC	AAGUGGGC
	5719	AGCGAUCC	CUGAUGA	X	GAA	AGGCCCAC	GUGGGCCUU	GGAUCGCU
	5724	AGCUUAGC	CUGAUGA	X	GAA	AUCCAAGG	CCUUGGAUC	GCUAAGCU
	5728	AGCCAGCU	CUGAUGA	X	GAA	AGCGAUCC	GGAUCGCUA	AGCUGGCU
	5737	AUCAAACA	CUGAUGA	X	GAA	AGCCAGCU	AGCUGGCUC	UGUUUGAU
30	5741	UAGCAUCA	CUGAUGA	X	GAA	ACAGAGCC	GGCUCUGUU	UGAUGCUA
	5742	AUAGCAUC					GCUCUGUUU	GAUGCUAU
						AGCAUCAA	UUGAUGCUA	UUUAUGCA
	5751	CUUGCAUA	CUGAUGA	X	GAA	AUAGCAUC	GAUGCUAUU	UAUGCAAG

	5752	ACUUGCAU	CUGAUGA	X	GAA	AAUAGCAU	AUGCUAUUU	AUGCAAGU
	57 53	AACUUGCA	CUGAUGA	X	GAA	AAAUAGCA	UGCUAUUUA	UGCAAGUU
	5761	UAGACCCU	CUGAUGA	X	GAA	ACUUGCAU	AUGCAAGUU	AGGGUCUA
	5762	AUAGACCC	CUGAUGA	X	GAA	AACUUGCA	UGCAAGUUA	GGGUCUAU
5	5767	AAUACAUA	CUGAUGA	X	GAA	ACCCUAAC	GUUAGGGUC	UAUGUAUU
	5769	UAAAUACA	CUGAUGA	X	GAA	AGACCCUA	UAGGGUCUA	UGUAUUUA
	5773	AUCCUAAA	CUGAUGA	X	GAA	ACAUAGAC	GUCUAUGUA	UUUAGGAU
	5 77 5	GCAUCCUA	CUGAUGA	X	GAA	AUACAUAG	CUAUGUAUU	UAGGAUGC
	5776	CGCAUCCU	CUGAUGA	x	GAA	AAUACAUA	UAUGUAUUU	AGGAUGCG
10	5777	GCGCAUCC	CUGAUGA	x	GAA	AAAUACAU	AUGUAUUUA	GGAUGCGC
	5788	CUGAAGAG	CUGAUGA	X	GAA	AGGCGCAU	AUGCGCCUA	CUCUUCAG
	5791	ACCCUGAA	CUGAUGA	X	GAA	AGUAGGCG	CGCCUACUC	UUCAGGGU
	5793	AGACCCUG	CUGAUGA	X	GAA	AGAGUAGG	CCUACUCUU	CAGGGUCU
	5794	UAGACCCU	CUGAUGA	X	GAA	AAGAGUAG	CUACUCUUC	AGGGUCUA
15	5800	GAUCUUUA	CUGAUGA	X	GAA	ACCCUGAA	UUCAGGGUC	UAAAGAUC
	5802	UUGAUCUU	CUGAUGA	X	GAA	AGACCCUG	CAGGGUCUA	AAGAUCAA
	5808	GCCCACUU	CUGAUGA	X	GAA	AUCUUUAG	CUAAAGAUC	AAGUGGGC
	5819	AGCGAUCC	CUGAUGA	X	GAA	AGGCCCAC	GUGGGCCUU	GGAUCGCU
	5824	AGCUUAGC	CUGAUGA	X	GAA	AUCCAAGG	CCUUGGAUC	GCUAAGCU
20	5828	AGCCAGCU	CUGAUGA	X	GAA	AGCGAUCC	GGAUCGCUA	AGCUGGCU
	5837	AUCAAACA	CUGAUGA	X	GAA	AGCCAGCU	AGCUGGCUC	UGUUUGAU
	5841	UAGCAUCA	CUGAUGA	X	GAA	ACAGAGCC	GGCUCUGUU	UGAUGCUA
	5842	AUAGCAUC	CUGAUGA	X	GAA	AACAGAGC	GCUCUGUUU	GAUGCUAU
	5849	UGCAUAAA	CUGAUGA	X	GAA	AGCAUCAA	UUGAUGCUA	UUUAUGCA
25	5851	CUUGCAUA	CUGAUGA	X	GAA	AUAGCAUC	GAUGCUAUU	UAUGCAAG
	5852	ACUUGCAU	CUGAUGA	X	GAA	AAUAGCAU	AUGCUAUUU	AUGCAAGU
	5853	AACUUGCA	CUGAUGA	X	GAA	AAAUAGCA	UGCUAUUUA	UGCAAGUU
	5861	UAGACCCU	CUGAUGA	X	GAA	ACUUGCAU	AUGCAAGUU	AGGGUCUA
	5862	AUAGACCC	CUGAUGA	X	GAA	AACUUGCA	UGCAAGUUA	GGGUCUAU
30	5867	AAUACAUA	CUGAUGA	X	GAA	ACCCUAAC	GUUAGGGUC	UAUGUAUU
	5869	UAAAUACA	CUGAUGA	X	GAA	AGACCCUA	UAGGGUCUA	UGUAUUUA
	5873	AUCCUAAA	CUGAUGA	X	GAÀ	ACAUAGAC	GUCUAUGUA	UUUAGGAU
	5875	ACAUCCUA	CUGAUGA	X	GAA	AUACAUAG	CUAUGUAUU	UAGGAUGU

	5876	GACAUCCU	CUGAUGA	X	GAA	AAUACAUA	UAUGUAUUU	AGGAUGUC
	5877	AGACAUCC	CUGAUGA	X	GAA	AAAUACAU	AUGUAUUUA	GGAUGUCU
	5884	AAGGUGCA	CUGAUGA	X	GAA	ACAUCCUA	UAGGAUGUC	UGCACCUU
	5892	GGCUGCAG	CUGAUGA	X	GAA	AGGUGCAG	CUGCACCUU	CUGCAGCC
5	5893	UGGCUGCA	CUGAUGA	X	GAA	AAGGUGCA	UGCACCUUC	UGCAGCCA
	5904	CAGCUUCU	CUGAUGA	X	GAA	ACUGGCUG	CAGCCAGUC	AGAAGCUG
	593 0	GAAGCAGC	CUGAUGA	X	GAA	AUCCACUG	CAGUGGAUU	GCUGCUUC
	5937	UCCCCAAG	CUGAUGA	X	GAA	AGCAGCAA	UUGCUGCUU	CUUGGGGA
	5938	CUCCCCAA	CUGAUGA	X	GAA	AAGCAGCA	UGCUGCUUC	UUGGGGAG
10	5940	UUCUCCCC	CUGAUGA	X	GAA	AGAAGCAG	CUGCUUCUU	GGGGAGAA
	5953	AGGAAGCA	CUGAUGA	X	GAA	ACUCUUCU	AGAAGAGUA	UGCUUCCU
	5958	AUAAAAGG	CUGAUGA	X	GAA	AGCAUACU	AGUAUGCUU	CCUUUUAU
	5959	GAUAAAAG	CUGAUGA	X	GAA	AAGCAUAC	GUAUGCUUC	CUUUUAUC
	5962	AUGGAUAA	CUGAUGA	X	GAA	AGGAAGCA	UGCUUCCUU	UUAUCCAU
15	5963	CAUGGAUA	CUGAUGA	X	GAA	AAGGAAGC	GCUUCCUUU	UAUCCAUG
	5964	ACAUGGAU	CUGAUGA	X	GAA	AAAGGAAG	cuuccuuuu	AUCCAUGU
	5965	UACAUGGA	CUGAUGA	X	GAA	AAAAGGAA	UUCCUUUUA	UCCAUGUA
	5967	AUUACAUG	CUGAUGA	X	GAA	AUAAAAGG	CCUUUUAUC	CAUGUAAU
	5973	AGUUAAAU	CUGAUGA	X	GAA	ACAUGGAU	AUCCAUGUA	AUUUAACU
20	5976	UACAGUUA	CUGAUGA	X	GAA	AUUACAUG	CAUGUAAUU	UAACUGUA
	5977	CUACAGUU	CUGAUGA	X	GAA	AAUUACAU	AUGUAAUUU	AACUGUAG
	5978	UCUACAGU	CUGAUGA	X	GAA	AAAUUACA	UGUAAUUUA	ACUGUAGA
	5984	UCAGGUUC	CUGAUGA	X	GAA	ACAGUUAA	UUAACUGUA	GAACCUGA
	5996	GUUACUUA	CUGAUGA	X	GAA	AGCUCAGG	CCUGAGCUC	UAAGUAAC
25	5998	CGGUUACU	CUGAUGA	X	GAA	AGAGCUCA	UGAGCUCUA	AGUAACCG
	6002	ucuucggu	CUGAUGA	X	GAA	ACUUAGAG	CUCUAAGUA	ACCGAAGA
	6015	CAGAGGCA	CUGAUGA	X	GAA	ACAUUCUU	AAGAAUGUA	UGCCUCUG
	6021	UAAGAACA	CUGAUGA	X	GAA	AGGCAUAC	GUAUGCCUC	UGUUCUUA
	6025	CACAUAAG	CUGAUGA	X	GAA	ACAGAGGC	GCCUCUGUU	CUUAUGUG
30	6026	GCACAUAA	CUGAUGA	X	GAA	AACAGAGG	CCUCUGUUC	UUAUGUGC
	6028	UGGCACAU	CUGAUGA	X	GAA	AGAACAGA	ucuguucuu	AUGUGCCA
	6029	GUGGCACA	CUGAUGA	X	GAA	AAGAACAG	CUGUUCUUA	UGUGCCAC
	6040	UAAACAAG	CUGAUGA	X	GAA	AUGUGGCA	UGCCACAUC	CUUGUUUA

	6043	CUUUAAAC	CUGAUGA	X	GAA	AGGAUGUG	CACAUCCUU	GUUUAAAG
	6046	AGCCUUUA	CUGAUGA	X	GAA	ACAAGGAU	AUCCUUGUU	UAAAGGCU
	6047	GAGCCUUU	CUGAUGA	X	GAA	AACAAGGA	UCCUUGUUU	AAAGGCUC
	6048	AGAGCCUU	CUGAUGA	X	GAA	AAACAAGG	CCUUGUUUA	AAGGCUCU
5	6055	CAUACAGA	CUGAUGA	X	GAA	AGCCUUUA	UAAAGGCUC	UCUGUAUG
	6057	UUCAUACA	CUGAUGA	X	GAA	AGAGCCUU	AAGGCUCUC	UGUAUGAA
	6061	UCUCUUCA	CUGAUGA	X	GAA	ACAGAGAG	CUCUCUGUA	UGAAGAGA
	6079	GUGCUGAU	CUGAUGA	X	GAA	ACGGUCCC	GGGACCGUC	AUCAGCAC
	6082	AAUGUGCU	CUGAUGA	X	GAA	AUGACGGU	ACCGUCAUC	AGCACAUU
10	6090	CACUAGGG	CUGAUGA	X	GAA	AUGUGCUG	CAGCACAUU	CCCUAGUG
	6091	UCACUAGG	CUGAUGA	X	GAA	AAUGUGCU	AGCACAUUC	CCUAGUGA
	6095	AGGCUCAC	CUGAUGA	X	GAA	AGGGAAUG	CAUUCCCUA	GUGAGCCU
	6104	GGAGCCAG	CUGAUGA	X	GAA	AGGCUCAC	GUGAGCCUA	CUGGCUCC
	6111	GCUGCCAG	CUGAUGA	X	GAA	AGCCAGUA	UACUGGCUC	CUGGCAGC
15	6124	UUCCACAA	CUGAUGA	X	GAA	AGCCGCUG	CAGCGGCUU	UUGUGGAA
	6125	CUUCCACA	CUGAUGA	X	GAA	AAGCCGCU	AGCGGCUUU	UGUGGAAG
	6126	UCUUCCAC	CUGAUGA	X	GAA	AAAGCCGC	GCGGCUUUU	GUGGAAGA
	6137	UGGCUAGU	CUGAUGA	X	GAA	AGUCUUCC	GGAAGACUC	ACUAGCCA
	6141	CUUCUGGC	CUGAUGA	X	GAA	AGUGAGUC	GACUCACUA	GCCAGAAG
20	6166	GUGGAGAG	CUGAUGA	X	GAA	ACUGUCCC	GGGACAGUC	CUCUCCAC
	6169	UUGGUGGA	CUGAUGA	X	GAA	AGGACUGU	ACAGUCCUC	UCCACCAA
	6171	UCUUGGUG	CUGAUGA	X	GAA	AGAGGACU	AGUCCUCUC	CACCAAGA
	6181	UGGAUUUA	CUGAUGA	X	GAA	AUCUUGGU	ACCAAGAUC	UAAAUCCA
	6183	UUUGGAUU	CUGAUGA	X	GAA	AGAUCUUG	CAAGAUCUA	AAUCCAAA
25	6187	UUUGUUUG	CUGAUGA	X	GAA	AUUUAGAU	AUCUAAAUC	CAAACAAA
	6204	UCUGGCUC	CUGAUGA	X	GAA	AGCCUGCU	AGCAGGCUA	GAGCCAGA
	6226	ACAACAAA	CUGAUGA	X	GAA	AUUUGUCC	GGACAAAUC	UUUGUUGU
	6228	GAACAACA	CUGAUGA	X	GAA	AGAUUUGU	ACAAAUCUU	UGUUGUUC
	6229	GGAACAAC	CUGAUGA	X	GAA	AAGAUUUG	CAAAUCUUU	GUUGUUCC
30	6232	AGAGGAAC	CUGAUGA	X	GAA	ACAAAGAU	AUCUUUGUU	GUUCCUCU
	6235	AGAAGAGG	CUGAUGA	X	GAA	ACAACAAA	UUUGUUGUU	CCUCUUCU
	6236	AAGAAGAG	CUGAUGA	X	GAA	AACAACAA	UUGUUGUUC	CUCUUCUU
	6239	GUAAAGAA	CUGAUGA	X	GAA	AGGAACAA	UUGUUCCUC	UUCUUUAC

	6241	GUGUAAAG	CUGAUGA	X	GAA	AGAGGAAC	GUUCCUCUU	CUUUACAC
	6242	UGUGUAAA	CUGAUGA	X	GAA	AAGAGGAA	UUCCUCUUC	UUUACACA
	6244	UAUGUGUA	CUGAUGA	X	GAA	AGAAGAGG	CCUCUUCUU	UACACAUA
	6245	GUAUGUGU	CUGAUGA	X	GAA	AAGAAGAG	CUCUUCUUU	ACACAUAC
5	6246	CGUAUGUG	CUGAUGA	X	GAA	AAAGAAGA	UCUUCUUUA	CACAUACG
	6252	GGUUUGCG	CUGAUGA	X	GAA	AUGUGUAA	UUACACAUA	CGCAAACC
	6280	AUUUUAUAA	CUGAUGA	X	GAA	AUUGCCAG	CUGGCAAUU	UUAUAAAU
	6281	GAUUUAUA	CUGAUGA	X	GAA	AAUUGCCA	UGGCAAUUU	UAUAAAUC
	6282	UGAUUUAU	CUGAUGA	X	GAA	AAAUUGCC	GGCAAUUUU	AUAAAUCA
10	6283	CUGAUUUA	CUGAUGA	X	GAA	AAAAUUGC	GCAAUUUUA	UAAAUCAG
	62 85	ACCUGAUU	CUGAUGA	X	GAA	AUAAAAUU	AUUUUUAUA	AAUCAGGU
	6289	AGUUACCU	CUGAUGA	X	GAA	AUUUAUAA	UUAUAAAUC	AGGUAACU
	6294	CUUCCAGU	CUGAUGA	X	GAA	ACCUGAUU	AAUCAGGUA	ACUGGAAG
	6308	CUGAGUUU	CUGAUGA	X	GAA	ACCUCCUU	AAGGAGGUU	AAACUCAG
15	6309	UCUGAGUU	CUGAUGA	X	GAA	AACCUCCU	AGGAGGUUA	AACUCAGA
	6314	บบบบบบ	CUGAUGA	X	GAA	AGUUUAAC	GUUAAACUC	AGAAAAA
	6331	AAUUGACU	CUGAUGA	X	GAA	AGGUCUUC	GAAGACCUC	AGUCAAUU
	6335	AGAGAAUU	CUGAUGA	X	GAA	ACUGAGGU	ACCUCAGUC	AAUUCUCU
	6339	AAGUAGAG	CUGAUGA	X	GAA	AUUGACUG	CAGUCAAUU	CUCUACUU
20	6340	AAAGUAGA	CUGAUGA	X	GAA	AAUUGACU	AGUCAAUUC	UCUACUUU
	6342	AAAAAGUA	CUGAUGA	X	GAA	AGAAUUGA	UCAAUUCUC	UACUUUUU
	6344	AAAAAAAG	CUGAUGA	X	GAA	AGAGAAUU	AAUUCUCUA	CUUUUUUU
	6347	ААААААА	CUGAUGA	X	GAA	AGUAGAGA	UCUCUACUU	טטטטטטט
	6348	AAAAAAA	CUGAUGA	X	GAA	AAGUAGAG	CUCUACUUU	טטטטטטט
25	6349	AAAAAAA	CUGAUGA	x	GAA	AAAGUAGA	UCUACUUUU	עטטטטטטט
	635 0	ААААААА	CUGAUGA	X	GAA	AAAAGUAG	CUACUUUUU	טטטטטטט
	6351	AAAAAAA	CUGAUGA	X	GAA	AAAAAGUA	UACUUUUUU	טטטטטטט
	6352	AAAAAAA	CUGAUGA	X	GAA	AAAAAAGU	ACUUUUUUU	טטטטטטט
	6353	AAAAAAA	CUGAUGA	X	GAA	AAAAAAAG	cuuuuuuu	עעעעעעעע
30	6354	GAAAAAA	CUGAUGA	X	GAA	AAAAAAA	עעעעעעעעע	บบบบบบบ
	6355	GGAAAAA	CUGAUGA	X	GAA	AAAAAAA	עעעעעעעעעע	บบบบบบ
	63 56	UGGAAAAA	CUGAUGA	X	GAA	AAAAAAA	עעעעעעעעעע	UUUUUCCA
	6357	UUGGAAAA	CUGAUGA	x	GAA	AAAAAAA	טטטטטטטט	UUUUCCAA

	6358	UUUGGAAA	CUGAUGA	X	GAA	AAAAAAA	עטטטטטטטט	UUUCCAAA
	6359	AUUUGGAA	CUGAUGA	X	GAA	АААААА	עעעעעעעעע	UUCCAAAU
	6360	GAUUUGGA	CUGAUGA	X	GAA	AAAAAAA	עטטטטטטטט	UCCAAAUC
	6361	UGAUUUGG	CUGAUGA	X	GAA	ААААААА	טטטטטטטט	CCAAAUCA
5	6362	CUGAUUUG	CUGAUGA	X	GAA	AAAAAAA	טטטטטטטט	CAAAUCAG
	6368	UAUUAUCU	CUGAUGA	X	GAA	AUUUGGAA	UUCCAAAUC	AGAUAAUA
	6373	UGGGCUAU	CUGAUGA	X	GAA	AUCUGAUU	AAUCAGAUA	AUAGCCCA
	6376	UGCUGGGC	CUGAUGA	X	GAA	AUUAUCUG	CAGAUAAUA	GCCCAGCA
	6388	GUUAUCAC	CUGAUGA	X	GAA	AUUUGCUG	CAGCAAAUA	GUGAUAAC
10	6394	UUAUUUGU	CUGAUGA	X	GAA	AUCACUAU	AUAGUGAUA	ACAAAUAA
	6401	UAAGGUUU	CUGAUGA	X	GAA	AUUUGUUA	UAACAAAUA	AAACCUUA
	6408	GAACAGCU	CUGAUGA	X	GAA	AGGUUUUA	UAAAACCUU	AGCUGUUC
	6409	UGAACAGC	CUGAUGA	X	GAA	AAGGUUUU	AAAACCUUA	GCUGUUCA
	6415	AAGACAUG	CUGAUGA	X	GAA	ACAGCUAA	UUAGCUGUU	CAUGUCUU
15	6416	CAAGACAU	CUGAUGA	X	GAA	AACAGCUA	UAGCUGUUC	AUGUCUUG
	6421	GAAAUCAA	CUGAUGA	X	GAA	ACAUGAAC	GUUCAUGUC	UUGAUUUC
	6423	UUGAAAUC	CUGAUGA	X	GAA	AGACAUGA	UCAUGUCUU	GAUUUCAA
	6427	AUUAUUGA	CUGAUGA	X	GAA	AUCAAGAC	GUCUUGAUU	UCAAUAAU
	6428	AAUUAUUG	CUGAUGA	X	GAA	AAUCAAGA	UCUUGAUUU	CAAUAAUU
20	6429	UAAUUAUU	CUGAUGA	X	GAA	AAAUCAAG	CUUGAUUUC	AAUAAUUA
	6433	GAAUUAAU	CUGAUGA	X	GAA	AUUGAAAU	AUUUCAAUA	AUUAAUUC
	6436	UAAGAAUU	CUGAUGA	X	GAA	AUUAUUGA	UCAAUAAUU	AAUUCUUA
	6437	UUAAGAAU	CUGAUGA	X	GAA	AAUUAUUG	CAAUAAUUA	AUUCUUAA
	6440	UGAUUAAG	CUGAUGA	X	GAA	AUUAAUUA	UAAUUAAUU	CUUAAUCA
25	6441	AUGAUUAA	CUGAUGA	X	GAA	AAUUAAUU	AAUUAAUUC	UUAAUCAU
	6443	UAAUGAUU	CUGAUGA	X	GAA	AGAAUUAA	UUAAUUCUU	AAUCAUUA
	6444	UUAAUGAU	CUGAUGA	X	GAA	AAGAAUUA	UAAUUCUUA	AUCAUUAA
	6447	CUCUUAAU	CUGAUGA	X	GAA	AUUAAGAA	UUCUUAAUC	AUUAAGAG
	6450	GGUCUCUU	CUGAUGA	X	GAA	AUGAUUAA	UUAAUCAUU	AAGAGACC
30	6451	UGGUCUCU	CUGAUGA	X	GAA	AAUGAUUA	UAAUCAUUA	AGAGACCA
	6461	GUAUUUAU	CUGAUGA	X	GAA	AUGGUCUC	GAGACCAUA	AUAAAUAC
	6464	GGAGUAUU	CUGAUGA	X	GAA	AUUAUGGU	ACCAUAAUA	AAUACUCC
	6468	AAAAGGAG	CUGAUGA	X	GAA	AUUUAUUA	UAAUAAAUA	CUCCUUUU

	6471	UUGAAAAG	CUGAUGA	X	GAA	AGUAUUUA	UAAAUACUC	CUUUUCAA
	6474	CUCUUGAA	CUGAUGA	X	GAA	AGGAGUAU	AUACUCCUU	UUCAAGAG
	6475	UCUCUUGA	CUGAUGA	X	GAA	AAGGAGUA	UACUCCUUU	UCAAGAGA
	6476	UUCUCUUG	CUGAUGA	X	GAA	AAAGGAGU	ACUCCUUUU	CAAGAGAA
5	6477	υυυςυςυυ	CUGAUGA	x	GAA	AAAAGGAG	cuccuuuuc	AAGAGAAA
	6497	ACAAUUCU	CUGAUGA	X	GAA	AUGGUUUU	AAAACCAUU	AGAAUUGU
	6498	AACAAUUC	CUGAUGA	X	GAA	AAUGGUUU	AAACCAUUA	GAAUUGUU
	6503	UGAGUAAC	CUGAUGA	X	GAA	AUUCUAAU	AUUAGAAUU	GUUACUCA
	6506	AGCUGAGU	CUGAUGA	X	GAA	ACAAUUCU	AGAAUUGUU	ACUCAGCU
10	6507	GAGCUGAG	CUGAUGA	X	GAA	AACAAUUC	GAAUUGUUA	CUCAGCUC
	6510	AAGGAGCU	CUGAUGA	X	GAA	AGUAACAA	UUGUUACUC	AGCUCCUU
	6515	GUUUGAAG	CUGAUGA	Х	GAA	AGCUGAGU	ACUCAGCUC	CUUCAAAC
	6518	UGAGUUUG	CUGAUGA	X	GAA	AGGAGCUG	CAGCUCCUU	CAAACUCA
	6519	CUGAGUUU	CUGAUGA	X	GAA	AAGGAGCU	AGCUCCUUC	AAACUCAG
15	6525	ACAAACCU	CUGAUGA	Х	GAA	AGUUUGAA	UUCAAACUC	AGGUUUGU
	65 30	AUGCUACA	CUGAUGA	X	GAA	ACCUGAGU	ACUCAGGUU	UGUAGCAU
	6531	UAUGCUAC	CUGAUGA	X	GAA	AACCUGAG	CUCAGGUUU	GUAGCAUA
	6534	AUGUAUGC	CUGAUGA	X	GAA	ACAAACCU	AGGUUUGUA	GCAUACAU
	65 39	GACUCAUG	CUGAUGA	X	GAA	AUGCUACA	UGUAGCAUA	CAUGAGUC
20	6547	GAUGGAUG	CUGAUGA	X	GAA	ACUCAUGU	ACAUGAGUC	CAUCCAUC
	6551	GACUGAUG	CUGAUGA	X	GAA	AUGGACUC	GAGUCCAUC	CAUCAGUC
	6555	CUUUGACU	CUGAUGA	X	GAA	AUGGAUGG	CCAUCCAUC	AGUCAAAG
	6559	CAUUCUUU	CUGAUGA	X	GAA	ACUGAUGG	CCAUCAGUC	AAAGAAUG
	6570	CCAGAUGG	CUGAUGA	X	GAA	ACCAUUCU	AGAAUGGUU	CCAUCUGG
25	6571	UCCAGAUG	CUGAUGA	X	GAA	AACCAUUC	GAAUGGUUC	CAUCUGGA
	65 75	AGACUCCA	CUGAUGA	X	GAA	AUGGAACC	GGUUCCAUC	UGGAGUCU
	6582	UACAUUAA	CUGAUGA	X	GAA	ACUCCAGA	UCUGGAGUC	UUAAUGUA
	6584	UCUACAUU	CUGAUGA	X	GAA	AGACUCCA	UGGAGUCUU	AAUGUAGA
	6585	UUCUACAU	CUGAUGA	X	GAA	AAGACUCC	GGAGUCUUA	AUGUAGAA
30	6590	υυυςυυυς	CUGAUGA	X	GAA	ACAUUAAG	CUUAAUGUA	GAAAGAAA
	6609	AUUAUUAC	CUGAUGA	X	GAA	AGUCUCCA	UGGAGACUU	GUAAUAAU
	6612	CUCAUUAU	CUGAUGA	X	GAA	ACAAGUCU	AGACUUGUA	AUAAUGAG
	6615	UAGCUCAU	CUGAUGA	x	GAA	AUUACAAG	CUUGUAAUA	AUGAGCUA

82

UUUGUAAC CUGAUGA X GAA AGCUCAUU 6623 AAUGAGCUA GUUACAAA 6626 CACUUUGU CUGAUGA X GAA ACUAGCUC GAGCUAGUU ACAAAGUG 6627 GCACUUUG CUGAUGA X GAA AACUAGCU AGCUAGUUA CAAAGUGC UAAUGAAC CUGAUGA X GAA AGCACUUU 6637 AAAGUGCUU GUUCAUUA UUUUAAUG CUGAUGA X GAA ACAAGCAC 6640 GUGCUUGUU CAUUAAAA 6641 AUUUUAAU CUGAUGA X GAA AACAAGCA UGCUUGUUC AUUAAAAU 6644 GCUAUUUU CUGAUGA X GAA AUGAACAA UUGUUCAUU AAAAUAGC UGCUAUUU CUGAUGA X GAA AAUGAACA UGUUCAUUA AAAUAGCA 6650 UUCAGUGC CUGAUGA X GAA AUUUUAAU AUUAAAAUA GCACUGAA 10 CAUGUUUC CUGAUGA X GAA AUUUUCAG 6662 CUGAAAAUU GAAACAUG 6674 UAUCAGUU CUGAUGA X GAA AUUCAUGU ACAUGAAUU AACUGAUA 6675 UUAUCAGU CUGAUGA X GAA AAUUCAUG CAUGAAUUA ACUGAUAA 6682 UGGAAUAU CUGAUGA X GAA AUCAGUUA UAACUGAUA AUAUUCCA 6685 GAUUGGAA CUGAUGA X GAA AUUAUCAG CUGAUAAUA UUCCAAUC 15 6687 AUGAUUGG CUGAUGA X GAA AUAUUAUC GAUAAUAUU CCAAUCAU 6688 AAUGAUUG CUGAUGA X GAA AAUAUUAU AUAAUAUUC CAAUCAUU 6693 UGGCAAAU CUGAUGA X GAA AUUGGAAU AUUCCAAUC AUUUGCCA 6696 AAAUGGCA CUGAUGA X GAA AUGAUUGG CCAAUCAUU UGCCAUUU 6697 UAAAUGGC CUGAUGA X GAA AAUGAUUG CAAUCAUUU GCCAUUUA 20 6703 UUGUCAUA CUGAUGA X GAA AUGGCAAA UUUGCCAUU UAUGACAA 6704 UUUGUCAU CUGAUGA X GAA AAUGGCAA UUGCCAUUU AUGACAAA 6705 UUUUGUCA CUGAUGA X GAA AAAUGGCA UGCCAUUUA UGACAAAA UUAGUGCC CUGAUGA X GAA ACCAUUUU 6719 AAAAUGGUU GGCACUAA 6726 UUCUUUGU CUGAUGA X GAA AGUGCCAA UUGGCACUA ACAAAGAA 25 6743 CUGAAAGG CUGAUGA X GAA AGUGCUCG CGAGCACUU CCUUUCAG 6744 UCUGAAAG CUGAUGA X GAA AAGUGCUC GAGCACUUC CUUUCAGA 6747 AACUCUGA CUGAUGA X GAA AGGAAGUG CACUUCCUU UCAGAGUU 6748 AAACUCUG CUGAUGA X GAA AAGGAAGU ACUUCCUUU CAGAGUUU 6749 GAAACUCU CUGAUGA X GAA AAAGGAAG CUUCCUUUC AGAGUUUC 30 6755 AUCUCAGA CUGAUGA X GAA ACUCUGAA UUCAGAGUU UCUGAGAU 6756 UAUCUCAG CUGAUGA X GAA AACUCUGA UCAGAGUUU CUGAGAUA 6757 UUAUCUCA CUGAUGA X GAA AAACUCUG CAGAGUUUC UGAGAUAA 6764 ACGUACAU CUGAUGA X GAA AUCUCAGA UCUGAGAUA AUGUACGU

	6769	GUUCCACG	CUGAUGA	X	GAA	ACAUUAUC	GAUAAUGUA	CGUGGAAC
	6781	UCCACCCA	CUGAUGA	X	GAA	ACUGUUCC	GGAACAGUC	UGGGUGGA
	6814	AAGACACA	CUGAUGA	X	GAA	ACUUGCAC	GUGCAAGUC	UGUGUCUU
	6820	ACUGACAA	CUGAUGA	X	GAA	ACACAGAC	GUCUGUGUC	UUGUCAGU
5	6822	GGACUGAC	CUGAUGA	X	GAA	AGACACAG	CUGUGUCUU	GUCAGUCC
	6825	CUUGGACU	CUGAUGA	X	GAA	ACAAGACA	UGUCUUGUC	AGUCCAAG
	6829	ACUUCUUG	CUGAUGA	X	GAA	ACUGACAA	UUGUCAGUC	CAAGAAGU
	6851	CUAAAAUU	CUGAUGA	X	GAA	ACAUCUCG	CGAGAUGUU	AAUUUUAG
	6852	CCUAAAAU	CUGAUGA	X	GAA	AACAUCUC	GAGAUGUUA	AUUUUAGG
10	6855	GUCCCUAA	CUGAUGA	X	GAA	AUUAACAU	AUGUUAAUU	UUAGGGAC
	68 56	GGUCCCUA	CUGAUGA	X	GAA	AAUUAACA	UGUUAAUUU	UAGGGACC
	6857	GGGUCCCU	CUGAUGA	X	GAA	AAAUUAAC	GUUAAUUUU	AGGGACCC
	6858	CGGGUCCC	CUGAUGA	X	GAA	AAAUUAA	AUUUUAAUU	GGGACCCG
	6872	UAGGAAAC	CUGAUGA	X	GAA	AGGCACGG	CCGUGCCUU	GUUUCCUA
15	6875	GGCUAGGA	CUGAUGA	x	GAA	ACAAGGCA	UGCCUUGUU	UCCUAGCC
	68 76	GGGCUAGG	CUGAUGA	X	GAA	AACAAGGC	GCCUUGUUU	CCUAGCCC
	6877	UGGGCUAG	CUGAUGA	X	GAA	AAACAAGG	CCUUGUUUC	CUAGCCCA
	6880	UUGUGGGC	CUGAUGA	X	GAA	AGGAAACA	UGUUUCCUA	GCCCACAA
	6901	AUCUGUUU	CUGAUGA	X	GAA	AUGUUUGC	GCAAACAUC	AAACAGAU
20	6910	CUAGCGAG	CUGAUGA	X	GAA	AUCUGUUU	AAACAGAUA	CUCGCUAG
	6913	AGGCUAGC	CUGAUGA	X	GAA	AGUAUCUG	CAGAUACUC	GCUAGCCU
	6917	AAUGAGGC	CUGAUGA	X	GAA	AGCGAGUA	UACUCGCUA	GCCUCAUU
	6922	AUUUAAAU	CUGAUGA	X	GAA	AGGCUAGC	GCUAGCCUC	AUUUAAAU
	6925	UCAAUUUA	CUGAUGA	X	GAA	AUGAGGCU	AGCCUCAUU	UAAAUUGA
25	6926	AUCAAUUU	CUGAUGA	X	GAA	AAUGAGGC	GCCUCAUUU	AAAUUGAU
	6927	AAUCAAUU	CUGAUGA	X	GAA	AAAUGAGG	CCUCAUUUA	AAUUGAUU
	6931	CUUUAAUC	CUGAUGA	X	GAA	UAAAUUUA	UUAAAUU	GAUUAAAG
	6935	CCUCCUUU	CUGAUGA	X	GAA	AUCAAUUU	AAAUUGAUU	AAAGGAGG
	6936	UCCUCCUU	CUGAUGA	X	GAA	AAUCAAUU	AAUUGAUUA	AAGGAGGA
30	6951	CGGCCAAA	CUGAUGA	X	GAA	AUGCACUC	GAGUGCAUC	UUUGGCCG
	6953	GUCGGCCA	CUGAUGA	X	GAA	AGAUGCAC	GUGCAUCUU	UGGCCGAC
	6954	UGUCGGCC	CUGAUGA	X	GAA	AAGAUGCA	UGCAUCUUU	GGCCGACA
	6970	CACACAGU	CUGAUGA	x	GAA	ACACCACU	AGUGGUGUA	ACUGUGUG

	7026	AACACACA	CUGAUGA	Х	GAA	ACACCCAC	GUGGGUGUA	UGUGUGUU
	7034	AUGCACAA	CUGAUGA	X	GAA	ACACACAU	AUGUGUGUU	UUGUGCAU
	7035	UAUGCACA	CUGAUGA	X	GAA	AACACACA	UGUGUGUUU	UGUGCAUA
	7036	UUAUGCAC	CUGAUGA	X	GAA	AAACACAC	GUGUGUUUU	GUGCAUA
5	7043	UAAAUAGU	CUGAUGA	X	GAA	AUGCACAA	UUGUGCAUA	ACUAUUUA
	7047	UCCUUAAA	CUGAUGA	X	GAA	AGUUAUGC	GCAUAACUA	UUUAAGGA
	7049	UUUCCUUA	CUGAUGA	X	GAA	AUAGUUAU	AUAACUAUU	UAAGGAAA
	7050	GUUUCCUU	CUGAUGA	X	GAA	AAUAGUUA	UAACUAUUU	AAGGAAAC
	7051	AGUUUCCU	CUGAUGA	X	GAA	AAAUAGUU	AACUAUUUA	AGGAAACU
10	7065	AACUUUAA	CUGAUGA	X	GAA	AUUCCAGU	ACUGGAAUU	UUAAAGUU
	7066	UAACUUUA	CUGAUGA	X	GAA	AAUUCCAG	CUGGAAUUU	UAAAGUUA
	7067	GUAACUUU	CUGAUGA	X	GAA	AAAUUCCA	UGGAAUUUU	AAAGUUAC
	7068	AGUAACUU	CUGAUGA	X	GAA	AAAAUUCC	GGAAUUUUA	AAGUUACU
	7073	AUAAAAGU	CUGAUGA	X	GAA	ACUUUAAA	UUUAAAGUU	ACUUUUAU
15	7074	UAUAAAAG	CUGAUGA	X	GAA	AACUUUAA	UUAAAGUUA	CUUUUAUA
	7077	UUGUAUAA	CUGAUGA	X	GAA	AGUAACUU	AAGUUACUU	UUAUACAA
	7078	UUUGUAUA	CUGAUGA	X	GAA	AAGUAACU	AGUUACUUU	UAUACAAA
	7079	GUUUGUAU	CUGAUGA	X	GAA	AAAGUAAC	GUUACUUUU	AUACAAAC
	7080	GGUUUGUA	CUGAUGA	X	GAA	AAAAGUAA	UUACUUUUA	UACAAACC
20	7082	UUGGUUUG	CUGAUGA	X	GAA	AUAAAAGU	ACUUUUAUA	CAAACCAA
	7095	GUAGCAUA	CUGAUGA	X	GAA	AUUCUUGG	CCAAGAAUA	UAUGCUAC
	7097	CUGUAGCA	CUGAUGA	X	GAA	AUAUUCUU	AAGAAUAUA	UGCUACAC
	7102	UAUAUCUG	CUGAUGA	X	GAA	AGCAUAUA	UAUAUGCUA	CAGAUAUA
	7108	CUGUCUUA	CUGAUGA	X	GAA	AUCUGUAG	CUACAGAUA	UAAGACAG
25	7110	GUCUGUCU	CUGAUGA	X	GAA	AUAUCUGU	ACAGAUAUA	AGACAGAC
	7124	UAGGACCA	CUGAUGA	X	GAA	ACCAUGUC	GACAUGGUU	UGGUCCUA
	7125	AUAGGACC	CUGAUGA	X	GAA	AACCAUGU	ACAUGGUUU	GGUCCUAU
	7129	AAAUAUAG	CUGAUGA	X	GAA	ACCAAACC	GGUUUGGUC	CUAUAUUU
	7132	UAGAAAUA	CUGAUGA	X	GAA	AGGACCAA	UUGGUCCUA	UAUUUCUA
30	7134	ACUAGAAA	CUGAUGA	X	GAA	AUAGGACC	GGUCCUAUA	UUUCUAGU
	7136	UGACUAGA	CUGAUGA	X	GAA	AUAUAGGA	UCCUAUAUU	UCUAGUCA
	7137	AUGACUAG	CUGAUGA	X	GAA	AAUAUAGG	CCUAUAUUU	CUAGUCAU
	7138	CAUGACUA	CUGAUGA	X	GAA	AAAUAUAG	CUAUAUUUC	UAGUCAUC

	22.40		GUGAUGA	v	C	AGAAAUAU		CHCAHCAH
	7140						AUAUUUCUA	
	7143	UUCAUCAU					UUUCUAGUC	
	7155	AUACAAAA	CUGAUGA	Х	GAA	ACAUUCAU	AUGAAUGUA	UUUUGUAU
	7157	GUAUACAA	CUGAUGA	X	GAA	AUACAUUC	GAAUGUAUU	UUGUAUAC
5	7158	GGUAUACA	CUGAUGA	X	GAA	AAUACAUU	AAUGUAUUU	UGUAUACC
	7159	UGGUAUAC	CUGAUGA	X	GAA	AAAUACAU	AUGUAUUUU	GUAUACCA
	7162	AGAUGGUA	CUGAUGA	X	GAA	ACAAAAUA	UAUUUUGUA	UACCAUCU
	7164	GAAGAUGG	CUGAUGA	X	GAA	AUACAAAA	UUUUGUAUA	CCAUCUUC
	7169	UAUAUGAA	CUGAUGA	X	GAA	AUGGUAUA	UAUACCAUC	UUCAUAUA
10	7171	AUUAUAUG	CUGAUGA	X	GAA	AGAUGGUA	UACCAUCUU	CAUAUAAU
	7172	UAUUAUAU	CUGAUGA	X	GAA	AAGAUGGU	ACCAUCUUC	AUAUAAUA
	7175	GUAUAUUA	CUGAUGA	X	GAA	AUGAAGAU	AUCUUCAUA	UAAUAUAC
	7177	AAGUAUAU	CUGAUGA	X	GAA	AUAUGAAG	CUUCAUAUA	AUAUACUU
	7180	UUUAAGUA	CUGAUGA	X	GAA	AUUAUAUG	CAUAUAAUA	UACUUAAA
15	7182	UUUUUAAG	CUGAUGA	X	GAA	AUAUUAUA	UAUAAUAUA	CUUAAAAA
	7185	AUAUUUUU	CUGAUGA	X	GAA	AGUAUAUU	AAUAUACUU	UAUAAAAA
	7186	UUUUAUAA	CUGAUGA	X	GAA	AAGUAUAU	AUAUACUUA	UUAUAAAA
	7192	UUAAGAAA	CUGAUGA	X	GAA	AAUUUUUA	AUAAAAUU	UUUCUUAA
	7194	AAUUAAGA	CUGAUGA	X	GAA	AUAUUUUU	UUAUAAAAA	UCUUAAUU
20	7195	CAAUUAAG	CUGAUGA	X	GAA	UUUUAUAA	AAAAUAUUU	CUUAAUUG
	7196	CCAAUUAA	CUGAUGA	X	GAA	UUUAUAAA	AAAUAUUUC	UUAAUUGG
	7198	UCCCAAUU	CUGAUGA	X	GAA	AGAAAUAU	AUAUUUCUU	AAUUGGGA
	719 9	AUCCCAAU	CUGAUGA	X	GAA	AAGAAAUA	UAUUUCUUA	AUUGGGAU
	7202	CAAAUCCC	CUGAUGA	X	GAA	AUUAAGAA	UUCUUAAUU	GGGAUUUG
25	7208	CGAUUACA	CUGAUGA	X	GAA	AUCCCAAU	AUUGGGAUU	UGUAAUCG
	7209	ACGAUUAC	CUGAUGA	X	GAA	AAUCCCAA	UUGGGAUUU	GUAAUCGU
	7212	GGUACGAU	CUGAUGA	X	GAA	ACAAAUCC	GGAUUUGUA	AUCGUACC
	7215	GUUGGUAC	CUGAUGA	X	GAA	AUUACAAA	UUUGUAAUC	GUACCAAC
	7218	UAAGUUGG	CUGAUGA	X	GAA	ACGAUUAC	GUAAUCGUA	CCAACUUA
30	7225	UAUCAAUU	CUGAUGA	X	GAA	AGUUGGUA	UACCAACUU	AAUUGAUA
	7226	UUAUCAAU	CUGAUGA	X	GAA	AAGUUGGU	ACCAACUUA	AUUGAUAA
	7229	AGUUUAUC	CUGAUGA	X	GAA	AUUAAGUU	AACUUAAUU	GAUAAACU
	7233	GCCAAGUU	CUGAUGA	X	GAA	AUCAAUUA	UAAUUGAUA	AACUUGGC

	1238	CAGUUGCC	CUGAUGA	Λ	GAA	AGUUUAUC	GAUAAACUU	GGCAACUG
	7249	GAACAUAA	CUGAUGA	X	GAA	AGCAGUUG	CAACUGCUU	UUAUGUUC
	7250	AGAACAUA	CUGAUGA	X	GAA	AAGCAGUU	AACUGCUUU	UAUGUUCU
	7251	CAGAACAU	CUGAUGA	X	GAA	AAAGCAGU	ACUGCUUUU	AUGUUCUG
5	7252	ACAGAACA	CUGAUGA	X	GAA	AAAAGCAG	CUGCUUUUA	UGUUCUGU
	7256	GGAGACAG	CUGAUGA	X	GAA	ACAUAAAA	UUUUAUGUU	CUGUCUCC
	7257	AGGAGACA	CUGAUGA	X	GAA	AACAUAAA	UUUAUGUUC	UGUCUCCU
	7261	UGGAAGGA	CUGAUGA	X	GAA	ACAGAACA	UGUUCUGUC	UCCUUCCA
	7263	UAUGGAAG	CUGAUGA	X	GAA	AGACAGAA	UUCUGUCUC	CUUCCAUA
10	7266	AUUUAUGG	CUGAUGA	X	GAA	AGGAGACA	UGUCUCCUU	CCAUAAAU
	7267	AAUUUAUG	CUGAUGA	X	GAA	AAGGAGAC	GUCUCCUUC	CAUAAAUU
	7271	GAAAAAUU	CUGAUGA	X	GAA	AUGGAAGG	CCUUCCAUA	AAUUUUUC
	7275	UUUUGAAA	CUGAUGA	X	GAA	AUUUAUGG	CCAUAAAUU	UUUCAAAA
	7276	AUUUUGAA	CUGAUGA	X	GAA	AAUUUAUG	CAUAAAUUU	UUCAAAAU
15	7277	UAUUUUGA	CUGAUGA	X	GAA	AAAUUUAU	AUAAAUUUU	UCAAAAUA
	7278	GUAUUUUG	CUGAUGA	X	GAA	AUUUAAAA	UUUUUAAAU	CAAAAUAC
	7279	AGUAUUUU	CUGAUGA	X	GAA	UUUAAAAA	AAAUUUUUC	AAAAUACU
	7285	UGAAUUAG	CUGAUGA	X	GAA	AUUUUGAA	UUCAAAAUA	CUAAUUCA
	7288	UGUUGAAU	CUGAUGA	X	GAA	AGUAUUUU	AAAAUACUA	AUUCAACA
20	7291	CUUUGUUG	CUGAUGA	X	GAA	AUUAGUAU	AUACUAAUU	CAACAAAG
	7292	UCUUUGUU	CUGAUGA	X	GAA	AAUUAGUA	UACUAAUUC	AACAAAGA
	7308	AAAAAAA	CUGAUGA	X	GAA	AGCUUUUU	AAAAAGCUC	טטטטטטטט
	7310	GGAAAAAA	CUGAUGA	X	GAA	AGAGCUUU	AAAGCUCUU	טטטטטטככ
	7311	AGGAAAAA	CUGAUGA	X	GAA	AAGAGCUU	AAGCUCUUU	UUUUUCCU
2 5	7312	UAGGAAAA	CUGAUGA	X	GAA	AAAGAGCU	AGCUCUUUU	UUUUCCUA
	7313	UUAGGAAA	CUGAUGA	X	GAA	AAAAGAGC	GCUCUUUUU	UUUCCUAA
	7314	UUUAGGAA	CUGAUGA	X	GAA	AAAAAGAG	cucuuuuu	UUCCUAAA
	7315	UUUUAGGA	CUGAUGA	X	GAA	AAAAAAGA	บดบบบบบบบ	UCCUAAAA
	7316	AUUUUAGG	CUGAUGA	X	GAA	AAAAAAG	cuuuuuuu	CCUAAAAU
30	7317	UAUUUUAG	CUGAUGA	X	GAA	AAAAAAA	uuuuuuuc	CUAAAAUA
	7320	GUUUAUUU	CUGAUGA	X	GAA	AGGAAAAA	UUUUUCCUA	AAAUAAAC
	7325	UUUGAGUU	CUGAUGA	X	GAA	AUUUUAGG	CCUAAAAUA	AACUCAAA
	7330	AUAAAUUU	CUGAUGA	X	GAA	AGUUUAUU	AAUAAACUC	AAAUUUA

	7335	CAAGGAUA	CUGAUGA	X	GAA	AUUUGAGU	ACUCAAAUU	UAUCCUUG
	7336	ACAAGGAU	CUGAUGA	X	GAA	AAUUUGAG	CUCAAAUUU	AUCCUUGU
	7337	AACAAGGA	CUGAUGA	X	GAA	AAAUUUGA	UCAAAUUUA	UCCUUGUU
	7339	UAAACAAG	CUGAUGA	X	GAA	AUAAAUUU	AAAUUUAUC	CUUGUUUA
5	7342	CUCUAAAC	CUGAUGA	X	GAA	AGGAUAAA	UUUAUCCUU	GUUUAGAG
	7345	CUGCUCUA	CUGAUGA	X	GAA	ACAAGGAU	AUCCUUGUU	UAGAGCAG
	7346	UCUGCUCU	CUGAUGA	X	GAA	AACAAGGA	UCCUUGUUU	AGAGCAGA
	7347	CUCUGCUC	CUGAUGA	X	GAA	AAACAAGG	CCUUGUUUA	GAGCAGAG
	7362	טטטטטכטט	CUGAUGA	X	GAA	AUUUUUCU	AGAAAAUU	AAGAAAAA
10	7363	GUUUUUCU	CUGAUGA	X	GAA	AAUUUUUC	GAAAAAUUA	AGAAAAAC
	7373	CCAUUUCA	CUGAUGA	X	GAA	AGUUUUUC	GAAAAACUU	UGAAAUGG
	7374	ACCAUUUC	CUGAUGA	X	GAA	AAGUUUUU	AAAAACUUU	GAAAUGGU
	7383	UUUUUUGA	CUGAUGA	X	GAA	ACCAUUUC	GAAAUGGUC	UCAAAAAA
	7385	AAUUUUUU	CUGAUGA	X	GAA	AGACCAUU	AAUGGUCUC	UUAAAAAA
15	7393	UAUUUAGC	CUGAUGA	X	GAA	AUUUUUUG	CAAAAAAUU	GCUAAAUA
	7397	AAAAUAUU	CUGAUGA	X	GAA	AGCAAUUU	AAAUUGCUA	UUUUAUAA
	7401	AUUGAAAA	CUGAUGA	X	GAA	AUUUAGCA	UGCUAAAUA	UUUUCAAU
	7403	CCAUUGAA	CUGAUGA	X	GAA	AUAUUUAG	CUAAAUAUU	UUCAAUGG
	7404	UCCAUUGA	CUGAUGA	X	GAA	AUUUUA	UUUAUAAAU	UCAAUGGA
20	7405	UUCCAUUG	CUGAUGA	X	GAA	AAAUAUUU	AAAUAUUUU	CAAUGGAA
	7406	UUUCCAUU	CUGAUGA	X	GAA	AAAAUAUU	AAUAUUUUC	AAUGGAAA
	7418	CUAACAUU	CUGAUGA	X	GAA	AGUUUUCC	GGAAAACUA	AAUGUUAG
	7424	GCUAAACU	CUGAUGA	X	GAA	ACAUUUAG	CUAAAUGUU	AGUUUAGC
	7425	AGCUAAAC	CUGAUGA	X	GAA	AACAUUUA	UAAAUGUUA	GUUUAGCU
25	7428	AUCAGCUA	CUGAUGA	X	GAA	ACUAACAU	AUGUUAGUU	UAGCUGAU
	7429	AAUCAGCU	CUGAUGA	X	GAA	AACUAACA	UGUUAGUUU	AGCUGAUU
	7430	CAAUCAGC	CUGAUGA	X	GAA	AAACUAAC	GUUAGUUUA	GCUGAUUG
	7437	CCCCAUAC	CUGAUGA	X	GAA	AUCAGCUA	UAGCUGAUU	GUAUGGGG
	7440	AAACCCCA	CUGAUGA	X	GAA	ACAAUCAG	CUGAUUGUA	UGGGGUUU
30	7447	GGUUCGAA	CUGAUGA	X	GAA	ACCCCAUA	UAUGGGGUU	UUCGAACC
	7448	AGGUUCGA	CUGAUGA	X	GAA	AACCCCAU	AUGGGGUUU	UCGAACCU
	7449	AAGGUUCG	CUGAUGA	X	GAA	AAACCCCA	UGGGGUUUU	CGAACCUU
	7450	AAAGGUUC	CUGAUGA	X	GAA	AAAACCCC	GGGGUUUUC	GAACCUUU

	7457	AAAAGUGA	CUGAUGA	X	GAA	AGGUUCGA	UCGAACCUU	UCACUUUU
	7458	AAAAAGUG	CUGAUGA	X	GAA	AAGGUUCG	CGAACCUUU	CACUUUUU
	7459	CAAAAAGU	CUGAUGA	X	GAA	AAAGGUUC	GAACCUUUC	ACUUUUUG
	7463	CAAACAAA	CUGAUGA	X	GAA	AGUGAAAG	CUUUCACUU	UUUGUUUG
5	7464	ACAAACAA	CUGAUGA	X	GAA	AAGUGAAA	UUUCACUUU	บบเรียบบบเรีย
	7465	AACAAACA	CUGAUGA	X	GAA	AAAGUGAA	UUCACUUUU	UGUUUGUU
	7466	AAACAAAC	CUGAUGA	X	GAA	AAAAGUGA	UCACUUUUU	GUUUGUUU
	7469	GUAAAACA	CUGAUGA	X	GAA	ACAAAAAG	CUUUUUGUU	UGUUUUAC
	7470	GGUAAAAC	CUGAUGA	X	GAA	AACAAAAA	บบบบบฐบบบ	GUUUUACC
10	7473	AUAGGUAA	CUGAUGA	X	GAA	ACAAACAA	UUGUUUGUU	UUACCUAU
	7474	AAUAGGUA	CUGAUGA	X	GAA	AACAAACA	UGUUUGUUU	UACCUAUU
	7475	AAAUAGGU	CUGAUGA	X	GAA	AAACAAAC	GUUUGUUUU	ACCUAUUU
	7476	GAAAUAGG	CUGAUGA	X	GAA	AAAACAAA	UUUGUUUUA	CCUAUUUC
	7480	UUGUGAAA	CUGAUGA	X	GAA	AGGUAAAA	UUUUACCUA	UUUCACAA
15	7482	AGUUGUGA	CUGAUGA	X	GAA	AUAGGUAA	UUACCUAUU	UCACAACU
	7483	CAGUUGUG	CUGAUGA	X	GAA	AAUAGGUA	UACCUAUUU	CACAACUG
	7484	ACAGUUGU	CUGAUGA	X	GAA	AAAUAGGU	ACCUAUUUC	ACAACUGU
	7495	UGGCAAUU	CUGAUGA	X	GAA	ACACAGUU	AACUGUGUA	AAUUGCCA
	7499	UUAUUGGC	CUGAUGA	X	GAA	AUUUACAC	GUGUAAAUU	GCCAAUAA
20	7506	ACAGGAAU	CUGAUGA	X	GAA	AUUGGCAA	UUGCCAAUA	AUUCCUGU
	7509	UGGACAGG	CUGAUGA	X	GAA	AUUAUUGG	CCAAUAAUU	CCUGUCCA
	7510	AUGGACAG	CUGAUGA	X	GAA	AAUUAUUG	CAAUAAUUC	CUGUCCAU
	7515	UUUUCAUG	CUGAUGA	X	GAA	ACAGGAAU	AUUCCUGUC	CAUGAAAA
	7531	CACUGGAU	CUGAUGA	X	GAA	AUUUGCAU	AUGCAAAUU	AUCCAGUG
25	7532	ACACUGGA	CUGAUGA	X	GAA	AAUUUGCA	UGCAAAUUA	UCCAGUGU
	7534	CUACACUG	CUGAUGA	X	GAA	AUAAUUUG	CAAAUUAUC	CAGUGUAG
	7541	AAUAUAUC	CUGAUGA	X	GAA	ACACUGGA	UCCAGUGUA	GAUAUAUU
	7545	GUCAAAUA	CUGAUGA	X	GAA	AUCUACAC	GUGUAGAUA	UAUUUGAC
	7547	UGGUCAAA	CUGAUGA	X	GAA	AUAUCUAC	GUAGAUAUA	UUUGACCA
30	754 9	GAUGGUCA	CUGAUGA	X	GAA	AUAUAUCU	AGAUAUAUU	UGACCAUC
	7550	UGAUGGUC	CUGAUGA	X	GAA	AAUAUAUC	GAUAUAUUU	GACCAUCA
	75 57	CAUAGGGU	CUGAUGA	X	GAA	AUGGUCAA	UUGACCAUC	ACCCUAUG
	7563	AAUAUCCA	CUGAUGA	x	GAA	AGGGUGAU	AUCACCCUA	UGGAUAUU

	7569	CUAGCCAA	CUGAUGA	X	GAA	AUCCAUAG	CUAUGGAUA	UUGGCUAG
	7571	AACUAGCC	CUGAUGA	X	GAA	AUAUCCAU	AUGGAUAUU	GGCUAGUU
	7576	GGCAAAAC	CUGAUGA	X	GAA	AGCCAAUA	UAUUGGCUA	GUUUUGCC
	7579	AAAGGCAA	CUGAUGA	X	GAA	ACUAGCCA	UGGCUAGUU	UUGCCUUU
5	7580	UAAAGGCA	CUGAUGA	X	GAA	AACUAGCC	GGCUAGUUU	UGCCUUUA
	7581	AUAAAGGC	CUGAUGA	X	GAA	AAACUAGC	GCUAGUUUU	GCCUUUAU
	7586	GCUUAAUA	CUGAUGA	X	GAA	AGGCAAAA	UUUUGCCUU	UAUUAAGC
	7587	UGCUUAAU	CUGAUGA	X	GAA	AAGGCAAA	UUUGCCUUU	AUUAAGCA
	7588	UUGCUUAA	CUGAUGA	X	GAA	AAAGGCAA	UUGCCUUUA	UUAAGCAA
10	7590	AUUUGCUU	CUGAUGA	X	GAA	AUAAAGGC	GCCUUUAUU	AAGCAAAU
	7591	AAUUUGCU	CUGAUGA	X	GAA	AAUAAAGG	CCUUUAUUA	AGCAAAUU
	7599	CUGAAAUG	CUGAUGA	X	GAA	AUUUGCUU	AAGCAAAUU	CAUUUCAG
	7600	GCUGAAAU	CUGAUGA	X	GAA	AAUUUGCU	AGCAAAUUC	AUUUCAGC
	7603	CAGGCUGA	CUGAUGA	X	GAA	AUGAAUUU	AAAUUCAUU	UCAGCCUG
15	7604	UCAGGCUG	CUGAUGA	X	GAA	AAUGAAUU	AAUUCAUUU	CAGCCUGA
	7605	UUCAGGCU	CUGAUGA	X	GAA	AAAUGAAU	AUUCAUUUC	AGCCUGAA
	7617	UAUAGGCA	CUGAUGA	X	GAA	ACAUUCAG	CUGAAUGUC	UGCCUAUA
	7623	AGAAUAUA	CUGAUGA	X	GAA	AGGCAGAC	GUCUGCCUA	UAUAUUCU
	7625	AGAGAAUA	CUGAUGA	X	GAA	AUAGGCAG	CUGCCUAUA	UAUUCUCU
20	7627	GCAGAGAA	CUGAUGA	X	GAA	AUAUAGGC	GCCUAUAUA	UUCUCUGC
	7629	GAGCAGAG	CUGAUGA	X	GAA	AUAUAUAG	CUAUAUAUU	CUCUGCUC
	76 30	AGAGCAGA	CUGAUGA	X	GAA	AAUAUAUA	UAUAUAUUC	UCUGCUCU
	7632	AAAGAGCA	CUGAUGA	X	GAA	AGAAUAUA	UAUAUUCUC	UGCUCUUU
	7637	AAUACAAA	CUGAUGA	X	GAA	AGCAGAGA	UCUCUGCUC	UUUGUAUU
25	7639	AGAAUACA	CUGAUGA	X	GAA	AGAGCAGA	UCUGCUCUU	UGUAUUCU
	7640	GAGAAUAC	CUGAUGA	X	GAA	AAGAGCAG	CUGCUCUUU	GUAUUCUC
	7643	AAGGAGAA	CUGAUGA	X	GAA	ACAAAGAG	CUCUUUGUA	UUCUCCUU
	7645	CAAAGGAG	CUGAUGA	X	GAA	AUACAAAG	CUUUGUAUU	CUCCUUUG
	7646	UCAAAGGA	CUGAUGA	X	GAA	AAUACAAA	UUUGUAUUC	UCCUUUGA
30	7648	GUUCAAAG	CUGAUGA	X	GAA	AGAAUACA	UGUAUUCUC	CUUUGAAC
	7651	CGGGUUCA	CUGAUGA	X	GAA	AGGAGAAU	AUUCUCCUU	UGAACCCG
	7652	ACGGGUUC	CUGAUGA	X	GAA	AAGGAGAA	uucuccuuu	GAACCCGU
	7661	GAUGUUUU	CUGAUGA	X	GAA	ACGGGUUC	GAACCCGUU	AAAACAUC

90

7662 GGAUGUUU CUGAUGA X GAA AACGGGUU AACCCGUUA AAACAUCC
7669 UGCCACAG CUGAUGA X GAA AUGUUUUA UAAAACAUC CUGUGGCA
Where "X" represents stem II region of a HH ribozyme (Hertel et al., 1992 Nucleic Acids Res. 20 3252). The length of stem II
5 may be ≥ 2 base-pairs.

ഗ

quence
Se
rate
Subst
and
yme
Sibozyme a
pin R
tid
Hair
or-l
ecept
Re
VEGF
£1¢1
Human
III:
Table

	nt.	HP Ribozyme Sequence	Ce	Substrate
	Position	uc		
	16	CGGGGAGG AGAA GAGAGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	IGUGGUACAUUACCUGGUA	ccncnce ean canacace
ស	39	CCGCUCCG AGAA GCCGCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	GUGGUACAUUACCUGGUA	GCCGCCG GCU CGGAGCGG
	180	CCGCCAGA AGAA GUCCUC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	GUGGUACAUUACCUGGUA	GAGGACG GAC UCUGGCGG
	190	AACGACCC AGAA GCCAGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	IGUGGUACAUUACCUGGUA	ucuadca acc agancanu
	278	GCGCGCAC AGAA GGACCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	GUGGUACAUUACCUGGUA	geancan dan angageac
	290	GACAGCUG AGAA GCGCGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GUGGUACAUUACCUGGUA	GCGCGCU GCU CAGCUGUC
10	295	AAGCAGAC AGAA GAGCAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	IGUGGUACAUUACCUGGUA	CUGCUCA GCU GUCUGCUU
	298	GAGAAGCA AGAA GCUGAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	IGUGGUACAUUACCUGGUA	CUCAGCU GUC UGCUUCUC
	302	CUGUGAGA AGAA GACAGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GUGGUACAUUACCUGGUA	GCUGUCU GCU UCUCACAG
	420	CAUUUAUG AGAA GCUUCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	IGUGGUACAUUACCUGGUA	GGAAGCA GCC CAUAAAUG
	486	CUUCCACA AGAA GAUUUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	IGUGGUACAUUACCUGGUA	UAAAUCU GCC UGUGGAAG
15	537	UNUGCUUG AGAA GUGUUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GUGGUACAUUACCUGGUA	GAACACA GCU CAAGCAAA
	565	AUAUTUGC AGAA GUAGAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GUGGUACAUUACCUGGUA	UUCUACA GCU GCAAAUAU
	721	CGUAACCC AGAA GGGAAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	IGUGGUACAUUACCUGGUA	AUUCCCU GCC GGGUUACG
	786	CGUUJUCC AGAA GGGAUC ACCAGAGAAACACACGUJGUGGUACAUJACCUGGUA	GUGGUACAUVACCUGGUA	GAUCCCU GAU GGAAAACG
	863	CUUCACAG AGAA GAAGCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	IGUGGUACAUUACCUGGUA	GGCUUCU GAC CUGUGAAG

UGGAGCU GAU CACUCUAA

UNAGAGUG AGAA GCUCCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

2525

2625

2652

GAUAGGUA AGAA GUCUUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

GGAACUUC AGAA GGGUCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

AAAGACU GAC UACCUAUC

GAAGUUCC

GAU

GGACCCA

UNACCGGC CUCUAUGA CGCUAUUU GAU UUACGAAA CCGGCCCC AGACCCG GCU CUCUACCC AAAUCCU GAC UUGUACCG UGUGGCU GAC UCUAGAAU GAAAAAA GUGCCAAA AAAUGCC GAC GGAAGGAG GUC UUGCACAG GUU CCACCACU GAU CACUUGGU GCACGCU GUU UAUUGAAA GUU CAAGGAAC GAU GAC GCU GAAAUCU GCU GAC UVACCCU GAU AACCCCA UAUCACA GCAAGCG CUUACCG GUUUCCA AGCCUCA UGAAACU AUCAGCA CCUCACU GGGUAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCUUGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGUAAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AAAUAGCG AGAA GAUUUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGGUU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGAAAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGUAGAG AGAA GGGUCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGAUUU ACCAGAGAACACACGUUGUGGGAACAUUACCUGGUA GCCACA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUGAUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CUCCUUCC AGAA GCAUTUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUUUCA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA AGUGGUGG AGAA GCUGAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAGGCU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA UUUCAAUA AGAA GCGUGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUGAGG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA UUUUUUUC AGAA CGGUACAA AGAA AUUCUAGA AGAA AGAA UUUCGUAA AGAA CUGUGCAA AGAA AGAGCCGG AGAA UUUGGCAC AGAA ACCAAGUG AGAA GCCGGUAA AGAA UCAUAGAG AGAA GUUCCUUG 1056 1310 1389 1535 1566 1572 1824 1908 1949 1973 2275 2396 2490 1604 2321 1301 ហ 10 15

GCACUCU GUU GGCCUCUC

GAGAGGCC AGAA GAGUGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

3995

15

AAGCUCU GAU GAUGUCAG UCUGACG GUU UCUACAAG UUCCAGAA GAACCCC GAU UAUGUGAG GCCUGAGG CUGGACU GCU GGCACAGA UUCUCUGA CCGAAGUU GUGAGCG GCU CCCUUAUG GAC UGUGGCUG AAGCUCU GAU GACUGAGC UVAACCU GCU GGGAGCCU GAU GGUGAUUG AGCUCCG GCU UUCAGGAA GGUUUCUA GAU UUCUUACA UCUVACA GUU UUCAAGUG UCUAUCA GAU CAUGCUGG GAC GNC GNC AACUCCU GCC UAUUUCA GCU CGUGCCG GGCCNCN AAGAUCU GGAUUCU UUUUGCA AGUUCCU GAGGCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGAGCU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GAAUCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CUUGUAGA AGAA GUCAGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAUCUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUAAGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGAACU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CUCACAUA AGAA GGGUUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCAAAA ACCAGAGAAACACGCUGGUGGGGACAUUACCUGGUA GAUAGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUCCAG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA UCAGAGAA AGAA GGAGUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAAAUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAGCUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CAUAAGGG AGAA GCUCAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGCACG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GAGCUU ACCAGAGAAACACGCUUGUGGGAACAUUACCUGGUA GGUUAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AGGCUCCC AGAA UUCCUGAA AGAA CACUUGAA AGAA CCAGCAUG AGAA AGAA AACUUCGG AGAA CUGACAUC AGAA CAGCCACA AGAA AGAA AGAA AGAA UGUAAGAA AGAA UUCUGGAA AGAA AGAA ncnenecc GCUCAGUC UAGAAACC CCUCAGGC CAAUCACC 2816 2930 2963 3207 3245 3256 3287 3402 3580 3655 3810 3846 3873 2873 3157 3211 3641

10

വ

94

GAU GGACAGCG

AGGAGCA

CGCUGUCC AGAA GCUCCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

GAAUAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

CUGUGCAA AGAA

5233

5281

4905

CUCCUCAG AGAA GCAUUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

GUU UUGCACAG

UVAUUCU

CUGAGGAG

GAC

AAAUGCA

GCUCCCC GCC CCCAGACU CGGGGCU GUC UGAUGUCA GUCAGCAG UCUGCCAU CAUUCCA GCU GUGGGCAC CCU CCCCGCCC GCCCCCA GAC UACAACUC GGAGCCA GCU GCUUUUUG AGGACCA GUU UGAUUGAG GCCAGCU GCU UUUUGUGA CUUCCCU GCU CCAACCCC GAU CACCCAAU UGGGCCA GCC CUGCAGCC CAAAACCC CCUUCUAC GCU CUGACCCU GUU GCUGUCU GAU gcc GAC ccenecn AGGCCCA CUUCCCA CUGCACU CCCUGCA CAGCUCU UGACAUCA AGAA GCCCCG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GACAGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGCCU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA SUGCCCAC AGAA GGAAUG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCACGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA AGUCUGGG AGAA GGGAGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGGGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CAAAAAGC AGAA GGCUCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UCACAAAA AGAA GCUGGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGGUUGG AGAA GGGAAG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CUCAAUCA AGAA GGUCCU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA AUUGGGUG AGAA GUGCAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGCUGCAG AGAA GGCCCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCAGGG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GAGCUG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AGGGUCAG AGAA GGGAAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CUGCUGAC AGAA AGAA AGAA GGGCGGG AGAA AGAA GGGUUUUG AGAA AUGGCAGA GAGUUGUA GUAGAAGG 4100 4120 4135 4210 4217 4224 4382 4385 4104 4537 4628 4636 4573 4594 4866 4871 Ŋ 15 10

GAU UGUAUGGG

UUUAGCU

GCUAAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

CCCAUACA AGAA

7433

WO 97/15662

95

CCUUCAAA GUC UGGGUGGA CAAGAAGU GCU UUUNAUGUU AUGUNCU GUC UCCUUCCA ucuugggg CUUAGCU GUU CAUGUCUU UUCAACU GCU UUGAAACU UGAUGCUA UGGCUCU GUU UGAUGCUA CUUAUGUG UUUGUGGA CUCUCCAC GGCAAUUU GAGGGCU GAU GGAGGAAA GUC UCUAUACC GGGACCCA GGGACUCA GNC GUG GOO gcn GNC gcn GCU GOO ugccucu guu GCO UVACUCA CUUGUCA CAACACA neecncn GAUUGCU GGCAACU AGACCCC UGGGACA UGGAACA GGCAGCG UGUGACA UUCUCCA UGGAAGGA AGAA GAACAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCAAUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAGGCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCUGCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUCCCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AAAUUGCC AGAA GUCACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCUAAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UUUGAAGG AGAA GAGUAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUUCCA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA ACUUCUUG AGAA GACAAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUUGCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA UAGCAUCA AGAA GAGCCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAGCCA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUGUUG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGAGAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUUGAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UUUCCUCC AGAA GCCCUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGUCU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGUAUAGA AGAA UGAGUCCC AGAA AGUUUCAA AGAA CCCCAAGA AGAA CACAUAAG AGAA UCCACAAA AGAA AGAA AGAA AACAUAAA AGAA AGAA UAGCAUCA AGAA AGAA AAGACAUG UCCACCCA GUGGAGAG Jegenece 6778 6826 7245 7258 5319 5358 5622 5738 5838 5933 6022 6120 6163 6270 6412 6511 5392 5563 15 10

വ

CAUUUCA GCC UGAAUGUC AAUGUCU GCC UAUAUAUU AUUCUCU GCU CUUUGUAU AAUUCCU GUC CAUGAAAA UUUUCAUG AGAA GGAAUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GACAUUCA AGAA GAAAUG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AAUAUAUA AGAA GACAUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AUACAAAG AGAA GAGAAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA 9092 7512 7618 7633

Table IV: Human KDR VEGF Receptor-Hammerhead Ribozyme and Substrate Sequence

	nt.	нн	Ribozym	e	Sequ	ience	Subs	strate
	Posi-							
5	tion							
	21	CACAGGGC	CUGAUGA	X	GAA	ACGGCCAG	CUGGCCGUC	GCCCUGUG
	33	UCCACGCA	CUGAUGA	X	GAA	AGCCACAG	CUGUGGCUC	UGCGUGGA
	56	AACCCACA	CUGAUGA	X	GAA	AGGCGGCC	GGCCGCCUC	UGUGGGUU
	64	ACUAGGCA	CUGAUGA	X	GAA	ACCCACAG	CUGUGGGUU	UGCCUAGU
10	65	CACUAGGC	CUGAUGA	X	GAA	AACCCACA	UGUGGGUUU	GCCUAGUG
	70	AGAAACAC	CUGAUGA	X	GAA	AGGCAAAC	GUUUGCCUA	GUGUUUCU
	75	UCAAGAGA	CUGAUGA	X	GAA	ACACUAGG	CCUAGUGUU	UCUCUUGA
	76	AUCAAGAG	CUGAUGA	X	GAA	AACACUAG	CUAGUGUUU	CUCUUGAU
	77	GAUCAAGA	CUGAUGA	X	GAA	AAACACUA	UAGUGUUUC	UCUUGAUC
15	79	CAGAUCAA	CUGAUGA	X	GAA	AGAAACAC	GUGUUUCUC	UUGAUCUG
	81	GGCAGAUC	CUGAUGA	X	GAA	AGAGAAAC	GUUUCUCUU	GAUCUGCC
	85	CCUGGGCA	CUGAUGA	x	GAA	AUCAAGAG	CUCUUGAUC	UGCCCAGG
	96	UGUAUGCU	CUGAUGA	х	GAA	AGCCUGGG	CCCAGGCUC	AGCAUACA
	102	UCUUUUUG	CUGAUGA	X	GAA	AUGCUGAG	CUCAGCAUA	CAAAAAGA
20	114	AUUGUAAG	CUGAUGA	X	GAA	AUGUCUUU	AAAGACAUA	CUUACAAU
	117	UUAAUUGU	CUGAUGA	X	GAA	AGUAUGUC	GACAUACUU	ACAAUUAA
	118	CUUAAUUG	CUGAUGA	X	GAA	AAGUAUGU	ACAUACUUA	CAAUUAAG
	123	UUAGCCUU	CUGAUGA	X	GAA	AUUGUAAG	CUUACAAUU	AAGGCUAA
	124	AUUAGCCU	CUGAUGA	X	GAA	AAUUGUAA	UUACAAUUA	AGGCUAAU
25	130	AGUUGUAU	CUGAUGA	X	GAA	AGCCUUAA	UUAAGGCUA	AUACAACU
	133	AAGAGUUG	CUGAUGA	X	GAA	AUUAGCCU	AGGCUAAUA	CAACUCUU
	139	AAUUUGAA	CUGAUGA	X	GAA	AGUUGUAU	AUACAACUC	UUCAAAUU
	141	GUAAUUUG	CUGAUGA	X	GAA	AGAGUUGU	ACAACUCUU	CAAAUUAC
	142	AGUAAUUU	CUGAUGA	X	GAA	AAGAGUUG	CAACUCUUC	AAAUUACU
30	147	CUGCAAGU	CUGAUGA	X	GAA	AUUUGAAG	CUUCAAAUU	ACUUGCAG
	148	CCUGCAAG	CUGAUGA	X	GAA	AAUUUGAA	UUCAAAUUA	CUUGCAGG
	151	UCCCCUGC	CUGAUGA	X	GAA	AGUAAUUU	AAAUUACUU	GCAGGGGA

	170	GCCAGUCC	CUGAUGA	X	GAA	AGUCCCUC	GAGGGACUU	GGACUGGC
	180	UUGGGCCA	CUGAUGA	X	GAA	AGCCAGUC	GACUGGCUU	UGGCCCAA
	181	AUUGGGCC	CUGAUGA	X	GAA	AAGCCAGU	ACUGGCUUU	GGCCCAAU
	190	ACUCUGAU	CUGAUGA	X	GAA	AUUGGGCC	GGCCCAAUA	AUCAGAGU
5	193	GCCACUCU	CUGAUGA	X	GAA	AUUAUUGG	CCAAUAAUC	AGAGUGGC
	243	UUACAGAA	CUGAUGA	X	GAA	AGGCCAUC	GAUGGCCUC	UUCUGUAA
	245	UCUUACAG	CUGAUGA	X	GAA	AGAGGCCA	UGGCCUCUU	CUGUAAGA
	246	GUCUUACA	CUGAUGA	X	GAA	AAGAGGCC	GGCCUCUUC	UGUAAGAC
	250	GAGUGUCU	CUGAUGA	X	GAA	ACAGAAGA	UCUUCUGUA	AGACACUC
10	258	GGAAUUGU	CUGAUGA	X	GAA	AGUGUCUU	AAGACACUC	ACAAUUCC
	264	ACUUUUGG	CUGAUGA	X	GAA	AUUGUGAG	CUCACAAUU	CCAAAAGU
	265	CACUUUUG	CUGAUGA	X	GAA	AAUUGUGA	UCACAAUUC	CAAAAGUG
	276	UCAUUUCC	CUGAUGA	X	GAA	AUCACUUU	AAAGUGAUC	GGAAAUGA
	296	AGCACUUG	CUGAUGA	X	GAA	AGGCUCCA	UGGAGCCUA	CAAGUGCU
15	305	CCCGGUAG	CUGAUGA	X	GAA	AGCACUUG	CAAGUGCUU	CUACCGGG
	306	UCCCGGUA	CUGAUGA	X	GAA	AAGCACUU	AAGUGCUUC	UACCGGGA
	308	UUUCCCGG	CUGAUGA	X	GAA	AGAAGCAC	GUGCUUCUA	CCGGGAAA
	323	CCGAGGCC	CUGAUGA	X	GAA	AGUCAGUU	AACUGACUU	GGCCUCGG
	329	AAAUGACC	CUGAUGA	X	GAA	AGGCCAAG	CUUGGCCUC	GGUCAUUU
20	333	ACAUAAAU	CUGAUGA	X	GAA	ACCGAGGC	GCCUCGGUC	AUUUAUGU
	336	UAGACAUA	CUGAUGA	X	GAA	AUGACCGA	UCGGUCAUU	UAUGUCUA
	337	AUAGACAU	CUGAUGA	X	GAA	AAUGACCG	CGGUCAUUU	AUGUCUAU
	338	CAUAGACA	CUGAUGA	X	GAA	AAAUGACC	GGUCAUUUA	UGUCUAUG
	342	UGAACAUA	CUGAUGA	X	GAA	ACAUAAAU	AUUUAUGUC	UAUGUUCA
25	344	CUUGAACA	CUGAUGA	X	GAA	AGACAUAA	UUAUGUCUA	UGUUCAAG
	348	UAAUCUUG	CUGAUGA	X	GAA	ACAUAGAC	GUCUAUGUU	CAAGAUUA
	349	GUAAUCUU	CUGAUGA	X	GAA	AACAUAGA	UCUAUGUUC	AAGAUUAC
	355	AGAUCUGU	CUGAUGA	X	GAA	AUCUUGAA	UUCAAGAUU	ACAGAUCU
	356	GAGAUCUG	CUGAUGA	X	GAA	AAUCUUGA	UCAAGAUUA	CAGAUCUC
30	362	UAAAUGGA	CUGAUGA	X	GAA	AUCUGUAA	UUACAGAUC	UCCAUUUA
	364	AAUAAAUG	CUGAUGA	X	GAA	AGAUCUGU	ACAGAUCUC	CAUUUAUU
	368	AAGCAAUA	CUGAUGA	X	GAA	AUGGAGAU	AUCUCCAUU	UAUUGCUU
	369	GAAGCAAU	CUGAUGA	X	GAA	AAUGGAGA	UCUCCAUUU	AUUGCUUC

	370	AGAAGCAA	CUGAUGA	X	GAA	AAAUGGAG	CUCCAUUUA	UUGCUUCU
	372	ACAGAAGC	CUGAUGA	X	GAA	AUAAAUGG	CCAUUUAUU	GCUUCUGU
	376	ACUAACAG	CUGAUGA	x	GAA	AGCAAUAA	UUAUUGCUU	CUGUUAGU
	377	CACUAACA	CUGAUGA	x	GAA	AAGCAAUA	UAUUGCUUC	UGUUAGUG
5	381	UGGUCACU	CUGAUGA	x	GAA	ACAGAAGC	GCUUCUGUU	AGUGACCA
	382	UUGGUCAC	CUGAUGA	x	GAA	AACAGAAG	CUUCUGUUA	GUGACCAA
	399	AUGUACAC	CUGAUGA	X	GAA	ACUCCAUG	CAUGGAGUC	GUGUACAU
	404	CAGUAAUG	CUGAUGA	x	GAA	ACACGACU	AGUCGUGUA	CAUUACUG
	408	UUCUCAGU	CUGAUGA	х	GAA	AUGUACAC	GUGUACAUU	ACUGAGAA
10	409	GUUCUCAG	CUGAUGA	x	GAA	AAUGUACA	UGUACAUUA	CUGAGAAC
	438	AGACAUGG	CUGAUGA	X	GAA	AUCACCAC	GUGGUGAUU	CCAUGUCU
	439	GAGACAUG	CUGAUGA	X	GAA	AAUCACCA	UGGUGAUUC	CAUGUCUC
	445	GGACCCGA	CUGAUGA	X	GAA	ACAUGGAA	UUCCAUGUC	UCGGGUCC
	447	AUGGACCC	CUGAUGA	X	GAA	AGACAUGG	CCAUGUCUC	GGGUCCAU
15	452	UUGAAAUG	CUGAUGA	x	GAA	ACCCGAGA	UCUCGGGUC	CAUUUCAA
	456	AGAUUUGA	CUGAUGA	X	GAA	AUGGACCC	GGGUCCAUU	UCAAAUCU
	457	GAGAUUUG	CUGAUGA	X	GAA	AAUGGACC	GGUCCAUUU	CAAAUCUC
	458	UGAGAUUU	CUGAUGA	X	GAA	AAAUGGAC	GUCCAUUUC	AAAUCUCA
	463	CACGUUGA	CUGAUGA	x	GAA	AUUUGAAA	UUUCAAAUC	UCAACGUG
20	465	GACACGUU	CUGAUGA	x	GAA	AGAUUUGA	UCAAAUCUC	AACGUGUC
	473	CACAAAGU	CUGAUGA	X	GAA	ACACGUUG	CAACGUGUC	ACUUUGUG
	47 7	CUUGCACA	CUGAUGA	x	GAA	AGUGACAC	GUGUCACUU	UGUGCAAG
	478	UCUUGCAC	CUGAUGA	X	GAA	AAGUGACA	UGUCACUUU	GUGCAAGA
	488	UUUCUGGG	CUGAUGA	x	GAA	AUCUUGCA	UGCAAGAUA	CCCAGAAA
25	503	CAGGAACA	CUGAUGA	x	GAA	AUCUCUUU	AAAGAGAUU	UGUUCCUG
	504	UCAGGAAC	CUGAUGA	x	GAA	AAUCUCUU	AAGAGAUUU	GUUCCUGA
	507	CCAUCAGG	CUGAUGA	X	GAA	ACAAAUCU	AGAUUUGUU	CCUGAUGG
	508	ACCAUCAG	CUGAUGA	x	GAA	AACAAAUC	GAUUUGUUC	CUGAUGGU
	517	AAUUCUGU	CUGAUGA	x	GAA	ACCAUCAG	CUGAUGGUA	ACAGAAUU
30	525	UCCCAGGA	CUGAUGA	x	GAA	AUUCUGUU	AACAGAAUU	UCCUGGGA
	526	GUCCCAGG	CUGAUGA	x	GAA	AAUUCUGU	ACAGAAUUU	CCUGGGAC
	527	UGUCCCAG	CUGAUGA	x	GAA	AAAUUCUG	CAGAAUUUC	CUGGGACA
	548	GAAUAGUA	CUGAUGA	x	GAA	AGCCCUUC	GAAGGGCUU	UACUAUUC

	549	GGAAUAGU	CUGAUGA	X	GAA	AAGCCCUU	AAGGGCUUU	ACUAUUC
	550	GGGAAUAG	CUGAUGA	X	GAA	AAAGCCCU	AGGGCUUUA	CUAUUCCO
	553	GCUGGGAA	CUGAUGA	X	GAA	AGUAAAGC	GCUUUACUA	UUCCCAGO
	555	UAGCUGGG	CUGAUGA	X	GAA	AUAGUAAA	UUUACUAUU	CCCAGCUA
5	556	GUAGCUGG	CUGAUGA	X	GAA	AAUAGUAA	UUACUAUUC	CCAGCUA
	563	UGAUCAUG	CUGAUGA	X	GAA	AGCUGGGA	UCCCAGCUA	CAUGAUCA
	570	GCAUAGCU	CUGAUGA	x	GAA	AUCAUGUA	UACAUGAUC	AGCUAUGO
	575	UGCCAGCA	CUGAUGA	X	GAA	AGCUGAUC	GAUCAGCUA	UGCUGGCA
	588	UCACAGAA	CUGAUGA	X	GAA	ACCAUGCC	GGCAUGGUC	UUCUGUGA
10	590	CUUCACAG	CUGAUGA	x	GAA	AGACCAUG	CAUGGUCUU	CUGUGAAG
	591	GCUUCACA	CUGAUGA	X	GAA	AAGACCAU	AUGGUCUUC	UGUGAAGO
	60 6	UCAUCAUU	CUGAUGA	X	GAA	AUUUUUGC	GCAAAAAUU	AAUGAUGA
	607	UUCAUCAU	CUGAUGA	X	GAA	AAUUUUUG	CAAAAAUUA	AUGAUGA
	619	AGACUGGU	CUGAUGA	X	GAA	ACUUUCAU	AUGAAAGUU	ACCAGUC
15	620	UAGACUGG	CUGAUGA	X	GAA	AACUUUCA	UGAAAGUUA	CCAGUCUA
	626	ACAUAAUA	CUGAUGA	X	GAA	ACUGGUAA	UUACCAGUC	UAUUAUGU
	628	GUACAUAA	CUGAUGA	X	GAA	AGACUGGU	ACCAGUCUA	UUAUGUA
	630	AUGUACAU	CUGAUGA	X	GAA	AUAGACUG	CAGUCUAUU	AUGUACAU
	631	UAUGUACA	CUGAUGA	X	GAA	AAUAGACU	AGUCUAUUA	UGUACAUA
20	635	CAACUAUG	CUGAUGA	X	GAA	ACAUAAUA	UAUUAUGUA	CAUAGUUG
	639	ACGACAAC	CUGAUGA	X	GAA	AUGUACAU	AUGUACAUA	GUUGUCGU
	642	ACAACGAC	CUGAUGA	X	GAA	ACUAUGUA	UACAUAGUU	GUCGUUGU
	645	CCUACAAC	CUGAUGA	X	GAA	ACAACUAU	AUAGUUGUC	GUUGUAGO
	648	UACCCUAC	CUGAUGA	X	GAA	ACGACAAC	GUUGUCGUU	GUAGGGUA
25	651	CUAUACCC	CUGAUGA	X	GAA	ACAACGAC	GUCGUUGUA	GGGUAUAG
	656	AAAUCCUA	CUGAUGA	X	GAA	ACCCUACA	UGUAGGGUA	UAGGAUUU
	658	AUAAAUCC	CUGAUGA	X	GAA	AUACCCUA	UAGGGUAUA	GGAUUUA
	663	ACAUCAUA	CUGAUGA	X	GAA	AUCCUAUA	UAUAGGAUU	UAUGAUGU
	664	CACAUCAU	CUGAUGA	X	GAA	AAUCCUAU	AUAGGAUUU	AUGAUGUG
30	665	CCACAUCA	CUGAUGA	X	GAA	AAAUCCUA	UAGGAUUUA	UGAUGUGG
	675	GGACUCAG	CUGAUGA	X	GAA	ACCACAUC	GAUGUGGUU	CUGAGUC
	676	CGGACUCA	CUGAUGA	x	GAA	AACCACAU	AUGUGGUUC	UGAGUCCO
	682	AUGAGACG	CUGAUGA	x	GAA	ACUCAGAA	UUCUGAGUC	CGUCUCAU

	686	UUCCAUGA	CUGAUGA	X	GAA	ACGGACUC	GAGUCCGUC	UCAUGGAA
	688	AAUUCCAU	CUGAUGA	X	GAA	AGACGGAC	GUCCGUCUC	AUGGAAUU
	696	GAUAGUUC	CUGAUGA	X	GAA	AUUCCAUG	CAUGGAAUU	GAACUAUC
	702	CCAACAGA	CUGAUGA	X	GAA	AGUUCAAU	AUUGAACUA	UCUGUUGG
5	704	CUCCAACA	CUGAUGA	X	GAA	AUAGUUCA	UGAACUAUC	UGUUGGAG
	708	UUUUCUCC	CUGAUGA	X	GAA	ACAGAUAG	CUAUCUGUU	GGAGAAAA
	720	UUUAAGAC	CUGAUGA	X	GAA	AGCUUUUC	GAAAAGCUU	GUCUUAAA
	723	CAAUUUAA	CUGAUGA	X	GAA	ACAAGCUU	AAGCUUGUC	UUAAAUUG
	725	UACAAUUU	CUGAUGA	X	GAA	AGACAAGC	GCUUGUCUU	AAAUUGUA
10	726	GUACAAUU	CUGAUGA	X	GAA	AAGACAAG	CUUGUCUUA	AAUUGUAC
	730	UGCUGUAC	CUGAUGA	X	GAA	AUUUAAGA	UCUUAAAUU	GUACAGCA
	733	UCUUGCUG	CUGAUGA	X	GAA	ACAAUUUA	UAAAUUGUA	CAGCAAGA
	750	CCCACAUU	CUGAUGA	X	GAA	AGUUCAGU	ACUGAACUA	AAUGUGGG
	762	UUGAAGUC	CUGAUGA	X	GAA	AUCCCCAC	GUGGGGAUU	GACUUCAA
15	767	CCCAGUUG	CUGAUGA	X	GAA	AGUCAAUC	GAUUGACUU	CAACUGGG
	768	UCCCAGUU	CUGAUGA	X	GAA	AAGUCAAU	AUUGACUUC	AACUGGGA
	779	AAGAAGGG	CUGAUGA	X	GAA	AUUCCCAG	CUGGGAAUA	CCCUUCUU
	784	CUUCGAAG	CUGAUGA	X	GAA	AGGGUAUU	AAUACCCUU	CUUCGAAG
	785	GCUUCGAA	CUGAUGA	x	GAA	AAGGGUAU	AUACCCUUC	UUCGAAGC
20	787	AUGCUUCG	CUGAUGA	X	GAA	AGAAGGGU	ACCCUUCUU	CGAAGCAU
	788	GAUGCUUC	CUGAUGA	X	GAA	AAGAAGGG	cccuucuuc	GAAGCAUC
	796	CUUAUGCU	CUGAUGA	X	GAA	AUGCUUCG	CGAAGCAUC	AGCAUAAG
	802	AAGUUUCU	CUGAUGA	X	GAA	AUGCUGAU	AUCAGCAUA	AGAAACUU
	810	CGGUUUAC	CUGAUGA	X	GAA	AGUUUCUU	AAGAAACUU	GUAAACCG
25	813	UCUCGGUU	CUGAUGA	X	GAA	ACAAGUUU	AAACUUGUA	AACCGAGA
	825	UGGGUUUU	CUGAUGA	X	GAA	AGGUCUCG	CGAGACCUA	AAAACCCA
	836	CACUCCCA	CUGAUGA	X	GAA	ACUGGGUU	AACCCAGUC	UGGGAGUG
	857	UGCUCAAA	CUGAUGA	X	GAA	AUUUCUUC	GAAGAAAUU	UUUGAGCA
	858	GUGCUCAA	CUGAUGA	X	GAA	AAUUUCUU	AAGAAAUUU	UUGAGCAC
30	859	GGUGCUCA	CUGAUGA	. X	GAA	AAAUUUCU	AGAAAUUUU	UGAGCACC
	860	AGGUGCUC	CUGAUGA	X	GAA	AAAAUUUC	GAAAUUUUU	GAGCACCU
	869	CUAUAGUU	CUGAUGA	. X	GAA	AGGUGCUC	GAGCACCUU	AACUAUAG
	870	UCUAUAGU	CUGAUGA	. х	GAA	AAGGUGCU	AGCACCUUA	ACUAUAGA

	874	ACCAUCUA	CUGAUGA	X	GAA	AGUUAAGG	CCUUAACUA	UAGAUGGU
	876	ACACCAUC	CUGAUGA	X	GAA	AUAGUUAA	UUAACUAUA	GAUGGUGU
	885	CUCCGGGU	CUGAUGA	X	GAA	ACACCAUC	GAUGGUGUA	ACCCGGAG
	905	AGGUGUAC	CUGAUGA	X	GAA	AUCCUUGG	CCAAGGAUU	GUACACCU
5	908	CACAGGUG	CUGAUGA	X	GAA	ACAAUCCU	AGGAUUGUA	CACCUGUG
	923	GCCCACUG	CUGAUGA	X	GAA	AUGCUGCA	UGCAGCAUC	CAGUGGGC
	956	CCCUGACA	CUGAUGA	X	GAA	AUGUGCUG	CAGCACAUU	UGUCAGGG
	957	ACCCUGAC	CUGAUGA	X	GAA	AAUGUGCU	AGCACAUUU	GUCAGGGU
	960	UGGACCCU	CUGAUGA	X	GAA	ACAAAUGU	ACAUUUGUC	AGGGUCCA
10	966	UUUUCAUG	CUGAUGA	X	GAA	ACCCUGAC	GUCAGGGUC	CAUGAAAA
	979	AGCAACAA	CUGAUGA	X	GAA	AGGUUUUU	AAAAACCUU	UUGUUGCU
	980	AAGCAACA	CUGAUGA	X	GAA	AAGGUUUU	AAAACCUUU	UGUUGCUU
	981	AAAGCAAC	CUGAUGA	X	GAA	AAAGGUUU	AAACCUUUU	GUUGCUUU
	984	CCAAAAGC	CUGAUGA	X	GAA	ACAAAAGG	ccuuuuguu	GCUUUUGG
15	988	ACUUCCAA	CUGAUGA	X	GAA	AGCAACAA	UUGUUGCUU	UUGGAAGU
	98 9	CACUUCCA	CUGAUGA	X	GAA	AAGCAACA	uguugcuuu	UGGAAGUG
	990	CCACUUCC	CUGAUGA	x	GAA	AAAGCAAC	GUUGCUUUU	GGAAGUGG
	1007	CCACCAGA	CUGAUGA	X	GAA	AUUCCAUG	CAUGGAAUC	UCUGGUGG
	1009	UUCCACCA	CUGAUGA	X	GAA	AGAUUCCA	UGGAAUCUC	UGGUGGAA
20	1038	GGGAUUCU	CUGAUGA	X	GAA	ACACGCUC	GAGCGUGUC	AGAAUCCC
	1044	UUCGCAGG	CUGAUGA	X	GAA	AUUCUGAC	GUCAGAAUC	CCUGCGAA
	1055	AACCAAGG	CUGAUGA	X	GAA	ACUUCGCA	UGCGAAGUA	CCUUGGUU
	1059	GGGUAACC	CUGAUGA	X	GAA	AGGUACUU	AAGUACCUU	GGUUACCC
	1063	GGGUGGGU	CUGAUGA	X	GAA	ACCAAGGU	ACCUUGGUU	ACCCACCC
25	1064	GGGGUGGG	CUGAUGA	X	GAA	AACCAAGG	CCUUGGUUA	CCCACCCC
	1080	UACCAUUU	CUGAUGA	X	GAA	AUUUCUGG	CCAGAAAUA	AAAUGGUA
	1088	CAUUUUUA	CUGAUGA	X	GAA	ACCAUUUU	AAAAUGGUA	UAAAAAUG
	1090	UCCAUUUU	CUGAUGA	X	GAA	AUACCAUU	AAUGGUAUA	AAAAUGGA
	1101	UCAAGGGG	CUGAUGA	X	GAA	AUUCCAUU	AAUGGAAUA	CCCCUUGA
30	1107	UUGGACUC	CUGAUGA	X	GAA	AGGGGUAU	AUACCCCUU	GAGUCCAA
	1112	UGUGAUUG	CUGAUGA	x	GAA	ACUCAAGG	CCUUGAGUC	CAAUCACA
	1117	AAUUGUGU	CUGAUGA	X	GAA	AUUGGACU	AGUCCAAUC	ACACAAUU
	1125	CCCGCUUU	CUGAUGA	X	GAA	AUUGUGUG	CACACAAUU	AAAGCGGG

	1126	CCCCGCUU	CUGAUGA	x	GAA	AAUUGUGU	ACACAAUUA	AAGCGGGG
	1140	AUCGUCAG	CUGAUGA	x	GAA	ACAUGCCC	GGGCAUGUA	CUGACGAU
	1149	ACUUCCAU	CUGAUGA	x	GAA	AUCGUCAG	CUGACGAUU	AUGGAAGU
	1150	CACUUCCA	CUGAUGA	X	GAA	AAUCGUCA	UGACGAUUA	UGGAAGUG
5	1180	GACAGUGU	CUGAUGA	X	GAA	AUUUCCUG	CAGGAAAUU	ACACUGUC
	1181	UGACAGUG	CUGAUGA	X	GAA	AAUUUCCU	AGGAAAUUA	CACUGUCA
	1188	GUAAGGAU	CUGAUGA	X	GAA	ACAGUGUA	UACACUGUC	AUCCUUAC
	1191	UUGGUAAG	CUGAUGA	X	GAA	AUGACAGU	ACUGUCAUC	CUUACCAA
	1194	GGAUUGGU	CUGAUGA	x	GAA	AGGAUGAC	GUCAUCCUU	ACCAAUCC
10	1195	GGGAUUGG	CUGAUGA	X	GAA	AAGGAUGA	UCAUCCUUA	CCAAUCCC
	1201	UGAAAUGG	CUGAUGA	X	GAA	AUUGGUAA	UUACCAAUC	CCAUUUCA
	1206	UCCUUUGA	CUGAUGA	X	GAA	AUGGGAUU	AAUCCCAUU	UCAAAGGA
	1207	CUCCUUUG	CUGAUGA	X	GAA	AAUGGGAU	AUCCCAUUU	CAAAGGAG
	1208	UCUCCUUU	CUGAUGA	X	GAA	AAAUGGGA	UCCCAUUUC	AAAGGAGA
15	1233	ACCAGAGA	CUGAUGA	X	GAA	ACCACAUG	CAUGUGGUC	UCUCUGGU
	1235	CAACCAGA	CUGAUGA	X	GAA	AGACCACA	UGUGGUCUC	UCUGGUUG
	1237	CACAACCA	CUGAUGA	X	GAA	AGAGACCA	UGGUCUCUC	UGGUUGUG
	1242	ACAUACAC	CUGAUGA	X	GAA	ACCAGAGA	UCUCUGGUU	GUGUAUGU
	1247	GUGGGACA	CUGAUGA	X	GAA	ACACAACC	GGUUGUGUA	UGUCCCAC
20	1251	UGGGGUGG	CUGAUGA	X	GAA	ACAUACAC	GUGUAUGUC	CCACCCCA
	1263	UUCUCACC	CUGAUGA	X	GAA	AUCUGGGG	CCCCAGAUU	GGUGAGAA
	1274	AGAUUAGA	CUGAUGA	X	GAA	AUUUCUCA	UGAGAAAUC	UCUAAUCU
	1276	AGAGAUUA	CUGAUGA	X	GAA	AGAUUUCU	AGAAAUCUC	UAAUCUCU
	1278	GGAGAGAU	CUGAUGA	X	GAA	AGAGAUUU	AAAUCUCUA	AUCUCUCC
25	1281	ACAGGAGA	CUGAUGA	X	GAA	AUUAGAGA	UCUCUAAUC	UCUCCUGU
	1283	CCACAGGA	CUGAUGA	X	GAA	AGAUUAGA	UCUAAUCUC	UCCUGUGG
	1285	AUCCACAG	CUGAUGA	X	GAA	AGAGAUUA	UAAUCUCUC	CUGUGGAU
	1294	CUGGUAGG	CUGAUGA	X	GAA	AUCCACAG	CUGUGGAUU	CCUACCAG
	1295	ACUGGUAG	CUGAUGA	X	GAA	AAUCCACA	UGUGGAUUC	CUACCAGU
30	1298	CGUACUGG	CUGAUGA	X	GAA	AGGAAUCC	GGAUUCCUA	CCAGUACG
	1304	UGGUGCCG	CUGAUGA	X	GAA	ACUGGUAG	CUACCAGUA	CGGCACCA
	1315	CAGCGUUU	CUGAUGA	X	GAA	AGUGGUGC	GCACCACUC	AAACGCUG
	1330	AUAGACCG	CUGAUGA	X	GAA	ACAUGUCA	UGACAUGUA	CGGUCUAU

	1335	AUGGCAUA	CUGAUGA	X	GAA	ACCGUACA	UGUACGGUC	UAUGCCAU
	1337	GAAUGGCA	CUGAUGA	X	GAA	AGACCGUA	UACGGUCUA	UGCCAUUC
	1344	GGGGGAGG	CUGAUGA	X	GAA	AUGGCAUA	UAUGCCAUU	ccuccccc
	1345	CGGGGGAG	CUGAUGA	X	GAA	AAUGGCAU	AUGCCAUUC	CUCCCCCG
5	1348	AUGCGGGG	CUGAUGA	X	GAA	AGGAAUGG	CCAUUCCUC	CCCCGCAU
	1357	GUGGAUGU	CUGAUGA	X	GAA	AUGCGGGG	CCCCGCAUC	ACAUCCAC
	1362	UACCAGUG	CUGAUGA	X	GAA	AUGUGAUG	CAUCACAUC	CACUGGUA
	1370	ACUGCCAA	CUGAUGA	X	GAA	ACCAGUGG	CCACUGGUA	UUGGCAGU
	1372	CAACUGCC	CUGAUGA	X	GAA	AUACCAGU	ACUGGUAUU	GGCAGUUG
10	1379	CUUCCUCC	CUGAUGA	X	GAA	ACUGCCAA	UUGGCAGUU	GGAGGAAG
	1416	GUCACUGA	CUGAUGA	X	GAA	ACAGCUUG	CAAGCUGUC	UCAGUGAC
	1418	UUGUCACU	CUGAUGA	X	GAA	AGACAGCU	AGCUGUCUC	AGUGACAA
	1433	CACAAGGG	CUGAUGA	X	GAA	AUGGGUUU	AAACCCAUA	CCCUUGUG
	1438	UUCUUCAC	CUGAUGA	X	GAA	AGGGUAUG	CAUACCCUU	GUGAAGAA
15	1466	CUCCCUGG	CUGAUGA	X	GAA	AGUCCUCC	GGAGGACUU	CCAGGGAG
	1467	CCUCCCUG	CUGAUGA	X	GAA	AAGUCCUC	GAGGACUUC	CAGGGAGG
	1480	UUCAAUUU	CUGAUGA	X	GAA	AUUUCCUC	GAGGAAAUA	AAAUUGAA
	1485	UUAACUUC	CUGAUGA	X	GAA	UUAUUUA	UUAAAAUU	GAAGUUAA
	1491	UUAUUUUU	CUGAUGA	X	GAA	ACUUCAAU	AUUGAAGUU	AAAAAUAA
20	1492	UAUUUUUAU	CUGAUGA	X	GAA	AACUUCAA	UUGAAGUUA	UAAAAAU
	1495	UUGAUUUU	CUGAUGA	X	GAA	AUUAACUU	AAGUUAAUA	AAAAUCAA
	1501	AGCAAAUU	CUGAUGA	X	GAA	UAUUUUUAU	AUAAAAAUC	AAUUUGCU
	1505	UUAGAGCA	CUGAUGA	X	GAA	AUUGAUUU	AAAUCAAUU	UGCUCUAA
	1506	AUUAGAGC	CUGAUGA	X	GAA	AAUUGAUU	AAUCAAUUU	GCUCUAAU
25	1510	UUCAAUUA	CUGAUGA	X	GAA	AGCAAAUU	AAUUUGCUC	UAAUUGAA
	1512	CCUUCAAU	CUGAUGA	X	GAA	AGAGCAAA	UUUGCUCUA	AUUGAAGG
	1515	UUUCCUUC	CUGAUGA	X	GAA	AUUAGAGC	GCUCUAAUU	GAAGGAAA
	1536	AGGGUACU	CUGAUGA	X	GAA	ACAGUUUU	AAAACUGUA	AGUACCCU
	1540	AACAAGGG	CUGAUGA	X	GAA	ACUUACAG	CUGUAAGUA	CCCUUGUU
30	1545	UGGAUAAC	CUGAUGA	X	GAA	AGGGUACU	AGUACCCUU	GUUAUCCA
	1548	GCUUGGAU	CUGAUGA	X	GAA	ACAAGGGU	ACCCUUGUU	AUCCAAGC
	1549	CGCUUGGA	CUGAUGA	X	GAA	AACAAGGG	CCCUUGUUA	UCCAAGCG
	1551	GCCGCUUG	CUGAUGA	X	GAA	AUAACAAG	CUUGUUAUC	CAAGCGGC

	1568	ACAAAGCU	CUGAUGA	X	GAA	ACACAUUU	AAAUGUGUC	AGCUUUGU
	1573	UUUGUACA	CUGAUGA	x	GAA	AGCUGACA	UGUCAGCUU	UGUACAAA
	1574	AUUUGUAC	CUGAUGA	X	GAA	AAGCUGAC	GUCAGCUUU	GUACAAAU
	1577	CACAUUUG	CUGAUGA	x	GAA	ACAAAGCU	AGCUUUGUA	CAAAUGUG
5	1593	ACUUUGUU	CUGAUGA	x	GAA	ACCGCUUC	GAAGCGGUC	AACAAAGU
	1602	CCUCUCCC	CUGAUGA	X	GAA	ACUUUGUU	AACAAAGUC	GGGAGAGG
	1623	UGGAAGGA	CUGAUGA	x	GAA	AUCACCCU	AGGGUGAUC	UCCUUCCA
	1625	CGUGGAAG	CUGAUGA	X	GAA	AGAUCACC	GGUGAUCUC	CUUCCACG
	1628	UCACGUGG	CUGAUGA	X	GAA	AGGAGAUC	GAUCUCCUU	CCACGUGA
10	1629	GUCACGUG	CUGAUGA	X	GAA	AAGGAGAU	AUCUCCUUC	CACGUGAC
	1645	AAUUUCAG	CUGAUGA	X	GAA	ACCCCUGG	CCAGGGGUC	CUGAAAUU
	1653	UGCAAAGU	CUGAUGA	x	GAA	AUUUCAGG	CCUGAAAUU	ACUUUGCA
	1654	UUGCAAAG	CUGAUGA	X	GAA	AAUUUCAG	CUGAAAUUA	CUUUGCAA
	1657	AGGUUGCA	CUGAUGA	X	GAA	AGUAAUUU	AAAUUACUU	UGCAACCU
15	1658	CAGGUUGC	CUGAUGA	x	GAA	AAGUAAUU	AAUUACUUU	GCAACCUG
	1697	ACCACAAA	CUGAUGA	X	GAA	ACACGCUC	GAGCGUGUC	UUUGUGGU
	1699	GCACCACA	CUGAUGA	x	GAA	AGACACGC	GCGUGUCUU	UGUGGUGC
	1700	UGCACCAC	CUGAUGA	x	GAA	AAGACACG	CGUGUCUUU	GUGGUGCA
	1721	CAAACGUA	CUGAUGA	X	GAA	AUCUGUCU	AGACAGAUC	UACGUUUG
20	1723	CUCAAACG	CUGAUGA	X	GAA	AGAUCUGU	ACAGAUCUA	CGUUUGAG
	1727	GGUUCUCA	CUGAUGA	X	GAA	ACGUAGAU	AUCUACGUU	UGAGAACC
	1728	AGGUUCUC	CUGAUGA	X	GAA	AACGUAGA	UCUACGUUU	GAGAACCU
	1737	UACCAUGU	CUGAUGA	X	GAA	AGGUUCUC	GAGAACCUC	ACAUGGUA
	1745	CAAGCUUG	CUGAUGA	X	GAA	ACCAUGUG	CACAUGGUA	CAAGCUUG
25	1752	UGUGGGCC	CUGAUGA	X	GAA	AGCUUGUA	UACAAGCUU	GGCCCACA
	1765	GAUUGGCA	CUGAUGA	X	GAA	AGGCUGUG	CACAGCCUC	UGCCAAUC
	1773	CCCACAUG	CUGAUGA	X	GAA	AUUGGCAG	CUGCCAAUC	CAUGUGGG
	1787	GUGUGGGC	CUGAUGA	X	GAA	ACUCUCCC	GGGAGAGUU	GCCCACAC
	1800	UUCUUGCA	CUGAUGA	X	GAA	ACAGGUGU	ACACCUGUU	UGCAAGAA
30	1801	GUUCUUGC	CUGAUGA	X	GAA	AACAGGUG	CACCUGUUU	GCAAGAAC
	1811	GAGUAUCC	CUGAUGA	X	GAA	AGUUCUUG	CAAGAACUU	GGAUACUC
	1816	CCAAAGAG	CUGAUGA	X	GAA	AUCCAAGU	ACUUGGAUA	CUCUUUGG
	1819	UUUCCAAA	CUGAUGA	X	GAA	AGUAUCCA	UGGAUACUC	UUUGGAAA

	1821	AAUUUCCA	CUGAUGA	X	GAA	AGAGUAUC	GAUACUCUU	UGGAAAUU
	1822	CAAUUUCC	CUGAUGA	X	GAA	AAGAGUAU	AUACUCUUU	GGAAAUUG
	1829	UGGCAUUC	CUGAUGA	X	GAA	AUUUCCAA	UUGGAAAUU	GAAUGCCA
	1844	UAUUAGAG	CUGAUGA	X	GAA	ACAUGGUG	CACCAUGUU	CUCUAAUA
5	1845	CUAUUAGA	CUGAUGA	X	GAA	AACAUGGU	ACCAUGUUC	UCUAAUAG
	1847	UGCUAUUA	CUGAUGA	X	GAA	AGAACAUG	CAUGUUCUC	UAAUAGCA
	1849	UGUGCUAU	CUGAUGA	X	GAA	AGAGAACA	UGUUCUCUA	AUAGCACA
	1852	AUUUGUGC	CUGAUGA	X	GAA	AUUAGAGA	UCUCUAAUA	GCACAAAU
	1866	AUGAUCAA	CUGAUGA	X	GAA	AUGUCAUU	AAUGACAUU	UUGAUCAU
10	1867	CAUGAUCA	CUGAUGA	X	GAA	AAUGUCAU	AUGACAUUU	UGAUCAUG
	1868	CCAUGAUC	CUGAUGA	X	GAA	AAAUGUCA	UGACAUUUU	GAUCAUGG
	1872	AGCUCCAU	CUGAUGA	X	GAA	AUCAAAAU	AUUUUGAUC	AUGGAGCU
	1881	GCAUUCUU	CUGAUGA	X	GAA	AGCUCCAU	AUGGAGCUU	AAGAAUGC
	1882	UGCAUUCU	CUGAUGA	X	GAA	AAGCUCCA	UGGAGCUUA	AGAAUGCA
15	1892	CCUGCAAG	CUGAUGA	X	GAA	AUGCAUUC	GAAUGCAUC	CUUGCAGG
	1895	GGUCCUGC	CUGAUGA	X	GAA	AGGAUGCA	UGCAUCCUU	GCAGGACC
	1913	GGCAGACA	CUGAUGA	X	GAA	AGUCUCCU	AGGAGACUA	UGUCUGCC
	1917	GCAAGGCA	CUGAUGA	X	GAA	ACAUAGUC	GACUAUGUC	UGCCUUGC
	1923	UCUUGAGC	CUGAUGA	X	GAA	AGGCAGAC	GUCUGCCUU	GCUCAAGA
20	1927	CCUGUCUU	CUGAUGA	X	GAA	AGCAAGGC	GCCUUGCUC	AAGACAGG
	1954	GACCACGC	CUGAUGA	X	GAA	AUGUCUUU	AAAGACAUU	GCGUGGUC
	1962	AGCUGCCU	CUGAUGA	X	GAA	ACCACGCA	UGCGUGGUC	AGGCAGCU
	1971	AGGACUGU	CUGAUGA	X	GAA	AGCUGCCU	AGGCAGCUC	ACAGUCCU
	1977	CGCUCUAG	CUGAUGA	X	GAA	ACUGUGAG	CUCACAGUC	CUAGAGCG
25	1980	ACACGCUC	CUGAUGA	X	GAA	AGGACUGU	ACAGUCCUA	GAGCGUGU
	2001	UUUCCUGU	CUGAUGA	X	GAA	AUCGUGGG	CCCACGAUC	ACAGGAAA
	2020	UGUCGUCU	CUGAUGA	X	GAA	AUUCUCCA	UGGAGAAUC	AGACGACA
	2032	UUCCCCAA	CUGAUGA	X	GAA	ACUUGUCG	CGACAAGUA	UUGGGGAA
	2034	CUUUCCCC	CUGAUGA	X	GAA	AUACUUGU	ACAAGUAUU	GGGGAAAG
30	2046	GAGACUUC	CUGAUGA	X	GAA	AUGCUUUC	GAAAGCAUC	GAAGUCUC
	2052	GUGCAUGA	CUGAUGA	X	GAA	ACUUCGAU	AUCGAAGUC	UCAUGCAC
	2054	CCGUGCAU	CUGAUGA	X	GAA	AGACUUCG	CGAAGUCUC	AUGCACGG
	2066	GAUUCCCA	CUGAUGA	X	GAÄ	AUGCCGUG	CACGGCAUC	UGGGAAUC

	2074	UGGAGGG	CUGAUGA	X	GAA	AUUCCCAG	CUGGGAAUC	CCCCUCCA
	2080	GAUCUGUG	CUGAUGA	X	GAA	AGGGGGAU	AUCCCCCUC	CACAGAUC
	2088	AACCACAU	CUGAUGA	X	GAA	AUCUGUGG	CCACAGAUC	AUGUGGUU
	2096	UAUCUUUA	CUGAUGA	x	GAA	ACCACAUG	CAUGUGGUU	UAAAGAUA
5	2097	UUAUCUUU	CUGAUGA	X	GAA	AACCACAU	AUGUGGUUU	AAAGAUAA
	2098	AUUAUCUU	CUGAUGA	х	GAA	AAACCACA	UGUGGUUUA	AAGAUAAU
	2104	GGUCUCAU	CUGAUGA	х	GAA	AUCUUUAA	UUAAAGAUA	AUGAGACC
	2115	UCUUCUAC	CUGAUGA	x	GAA	AGGGUCUC	GAGACCCUU	GUAGAAGA
	2118	GAGUCUUC	CUGAUGA	x	GAA	ACAAGGGU	ACCCUUGUA	GAAGACUC
10	2126	CAAUGCCU	CUGAUGA	x	GAA	AGUCUUCU	AGAAGACUC	AGGCAUUG
	2133	UUCAAUAC	CUGAUGA	x	GAA	AUGCCUGA	UCAGGCAUU	GUAUUGAA
	2136	UCCUUCAA	CUGAUGA	x	GAA	ACAAUGCC	GGCAUUGUA	UUGAAGGA
	2138	CAUCCUUC	CUGAUGA	x	GAA	AUACAAUG	CAUUGUAUU	GAAGGAUG
	2160	CGGAUAGU	CUGAUGA	x	GAA	AGGUUCCG	CGGAACCUC	ACUAUCCG
15	2164	UCUGCGGA	CUGAUGA	х	GAA	AGUGAGG U	ACCUCACUA	UCCGCAGA
	2166	ACUCUGCG	CUGAUGA	X	GAA	AUAGUGAG	CUCACUAUC	CGCAGAGU
	2196	CAGGUGUA	CUGAUGA	X	GAA	AGGCCUUC	GAAGGCCUC	UACACCUG
	2198	GGCAGGUG	CUGAUGA	X	GAA	AGAGGCCU	AGGCCUCUA	CACCUGCC
	2220	CAGCCAAG	CUGAUGA	X	GAA	ACACUGCA	UGCAGUGUU	CUUGGCUG
20	2221	ACAGCCAA	CUGAUGA	x	GAA	AACACUGC	GCAGUGUUC	UUGGCUGU
	2223	GCACAGCC	CUGAUGA	X	GAA	AGAACACU	AGUGUUCUU	GGCUGUGC
	2246	UUAUGAAA	CUGAUGA	X	GAA	AUGCCUCC	GGAGGCAUU	UUUCAUAA
	2247	AUUAUGAA	CUGAUGA	X	GAA	AAUGCCUC	GAGGCAUUU	UUCAUAAU
	2248	UAUUAUGA	CUGAUGA	X	GAA	AAAUGCCU	AGGCAUUUU	UCAUAAUA
25	2249	CUAUUAUG	CUGAUGA	X	GAA	AAAAUGCC	GGCAUUUUU	CAUAAUAG
	2250	UCUAUUAU	CUGAUGA	X	GAA	AAAAAUGC	GCAUUUUUC	AUAAUAGA
	2253	CCUUCUAU	CUGAUGA	X	GAA	AUGAAAA	UUUUUCAUA	AUAGAAGG
	2256	GCACCUUC	CUGAUGA	X	GAA	AUUAUGAA	UUCAUAAUA	GAAGGUGC
	2282	UGAUUUCC	CUGAUGA	X	GAA	AGUUCGUC	GACGAACUU	GGAAAUCA
30	2289	AGAAUAAU	CUGAUGA	X	GAA	AUUUCCAA	UUGGAAAUC	AUUAUUCU
	2292	ACUAGAAU	CUGAUGA	X	GAA	AUGAUUUC	GAAAUCAUU	AUUCUAGU
	2293	UACUAGAA	CUGAUGA	X	GAA	AAUGAUUU	AAAUCAUUA	UUCUAGUA
	2295	CCUACUAG	CUGAUGA	X	GAA	AUAAUGAU	AUCAUUAUU	CUAGUAGG

	2296	GCCUACUA	CUGAUGA	X	GAA	AAUAAUGA	UCAUUAUUC	UAGUAGGC
	2298	GUGCCUAC	CUGAUGA	X	GAA	AGAAUAAU	AUUAUUCUA	GUAGGCAC
	2301	GUCGUGCC	CUGAUGA	X	GAA	ACUAGAAU	AUUCUAGUA	GGCACGAC
	2316	AACAUGGC	CUGAUGA	X	GAA	AUCACCGU	ACGGUGAUU	GCCAUGUU
5	2324	GCCAGAAG	CUGAUGA	X	GAA	ACAUGGCA	UGCCAUGUU	CUUCUGGC
	2325	AGCCAGAA	CUGAUGA	X	GAA	AACAUGGC	GCCAUGUUC	UUCUGGCU
	2327	GUAGCCAG	CUGAUGA	X	GAA	AGAACAUG	CAUGUUCUU	CUGGCUAC
	2328	AGUAGCCA	CUGAUGA	X	GAA	AAGAACAU	AUGUUCUUC	UGGCUACU
	2334	ACAAGAAG	CUGAUGA	X	GAA	AGCCAGAA	UUCUGGCUA	CUUCUUGU
10	2337	AUGACAAG	CUGAUGA	X	GAA	AGUAGCCA	UGGCUACUU	CUUGUCAU
	2338	GAUGACAA	CUGAUGA	X	GAA	AAGUAGCC	GGCUACUUC	UUGUCAUC
	2340	AUGAUGAC	CUGAUGA	X	GAA	AGAAGUAG	CUACUUCUU	GUCAUCAU
	2343	AGGAUGAU	CUGAUGA	X	GAA	ACAAGAAG	CUUCUUGUC	AUCAUCCU
	2346	CCUAGGAU	CUGAUGA	X	GAA	AUGACAAG	CUUGUCAUC	AUCCUAGG
15	2349	GUCCCUAG	CUGAUGA	X	GAA	AUGAUGAC	GUCAUCAUC	CUAGGGAC
	2352	ACGGUCCC	CUGAUGA	X	GAA	AGGAUGAU	AUCAUCCUA	GGGACCGU
	2361	GCCCGCUU	CUGAUGA	X	GAA	ACGGUCCC	GGGACCGUU	AAGCGGGC
	2362	GGCCCGCU	CUGAUGA	X	GAA	AACGGUCC	GGACCGUUA	AGCGGGCC
	2396	UGGACAAG	CUGAUGA	X	GAA	AGCCUGUC	GACAGGCUA	CUUGUCCA
20	239 9	CGAUGGAC	CUGAUGA	X	GAA	AGUAGCCU	AGGCUACUU	GUCCAUCG
	2402	UGACGAUG	CUGAUGA	X	GAA	ACAAGUAG	CUACUUGUC	CAUCGUCA
	2406	UCCAUGAC	CUGAUGA	X	GAA	AUGGACAA	UUGUCCAUC	GUCAUGGA
	2409	GGAUCCAU	CUGAUGA	X	GAA	ACGAUGGA	UCCAUCGUC	AUGGAUCC
	2416	UUCAUCUG	CUGAUGA	X	GAA	AUCCAUGA	UCAUGGAUC	CAGAUGAA
25	2427	UCCAAUGG	CUGAUGA	X	GAA	AGUUCAUC	GAUGAACUC	CCAUUGGA
	2432	GUUCAUCC	CUGAUGA	X	GAA	AUGGGAGU	ACUCCCAUU	GGAUGAAC
	2443	UCGUUCAC	CUGAUGA	X	GAA	AUGUUCAU	AUGAACAUU	GUGAACGA
	2458	GGCAUCAU	CUGAUGA	X	GAA	AGGCAGUC	GACUGCCUU	AUGAUGCC
	2459	UGGCAUCA	CUGAUGA	X	GAA	AAGGCAGU	ACUGCCUUA	UGAUGCCA
30	2480	CUCUGGGG	CUGAUGA	X	GAA	AUUCCCAU	AUGGGAAUU	CCCCAGAG
	2481	UCUCUGGG	CUGAUGA	x	GAA	AAUUCCCA	UGGGAAUUC	CCCAGAGA
	2502	GGCUUACC	CUGAUGA	x	GAA	AGGUUCAG	CUGAACCUA	GGUAAGCC
	2506	AAGAGGCU	CUGAUGA	X	GAA	ACCUAGGU	ACCUAGGUA	AGCCUCUU

	2512	ACGGCCAA	CUGAUGA	X	GAA	AGGCUUAC	GUAAGCCUC	UUGGCCGU
	2514	CCACGGCC	CUGAUGA	X	GAA	AGAGGCUU	AAGCCUCUU	GGCCGUGG
	2528	CUUGGCCA	CUGAUGA	x	GAA	AGGCACCA	UGGUGCCUU	UGGCCAAG
	2529	UCUUGGCC	CUGAUGA	X	GAA	AAGGCACC	GGUGCCUUU	GGCCAAGA
5	2541	UCUGCUUC	CUGAUGA	X	GAA	AUCUCUUG	CAAGAGAUU	GAAGCAGA
	2555	CAAUUCCA	CUGAUGA	X	GAA	AGGCAUCU	AGAUGCCUU	UGGAAUUG
	2556	UCAAUUCC	CUGAUGA	X	GAA	AAGGCAUC	GAUGCCUUU	GGAAUUGA
	2562	GUCUUGUC	CUGAUGA	X	GAA	AUUCCAAA	UUUGGAAUU	GACAAGAC
	2578	UGUCCUGC	CUGAUGA	x	GAA	AGUUGCUG	CAGCAACUU	GCAGGACA
10	2589	UUGACUGC	CUGAUGA	X	GAA	ACUGUCCU	AGGACAGUA	GCAGUCAA
	2595	AACAUUUU	CUGAUGA	X	GAA	ACUGCUAC	GUAGCAGUC	AAAAUGUU
	2603	CUUCUUUC	CUGAUGA	X	GAA	ACAUUUUG	CAAAAUGUU	GAAAGAAG
	2632	GAGAGCUC	CUGAUGA	x	GAA	AUGCUCAC	GUGAGCAUC	GAGCUCUC
	2638	AGACAUGA	CUGAUGA	X	GAA	AGCUCGAU	AUCGAGCUC	UCAUGUCU
15	2640	UCAGACAU	CUGAUGA	x	GAA	AGAGCUCG	CGAGCUCUC	AUGUCUGA
	2645	UGAGUUCA	CUGAUGA	X	GAA	ACAUGAGA	UCUCAUGUC	UGAACUCA
	2652	AGGAUCUU	CUGAUGA	x	GAA	AGUUCAGA	UCUGAACUC	AAGAUCCU
	2658	UGAAUGAG	CUGAUGA	X	GAA	AUCUUGAG	CUCAAGAUC	CUCAUUCA
	2661	AUAUGAAU	CUGAUGA	x	GAA	AGGAUCUU	AAGAUCCUC	AUUCAUAU
20	2664	CCAAUAUG	CUGAUGA	X	GAA	AUGAGGAU	AUCCUCAUU	CAUAUUGG
	2665	ACCAAUAU	CUGAUGA	x	GAA	AAUGAGGA	UCCUCAUUC	AUAUUGGU
	2668	GUGACCAA	CUGAUGA	X	GAA	AUGAAUGA	UCAUUCAUA	UUGGUCAC
	2670	UGGUGACC	CUGAUGA	X	GAA	AUAUGAAU	AUUCAUAUU	GGUCACCA
	2674	GAGAUGGU	CUGAUGA	X	GAA	ACCAAUAU	AUAUUGGUC	ACCAUCUC
25	2680	CACAUUGA	CUGAUGA	X	GAA	AUGGUGAC	GUCACCAUC	UCAAUGUG
	2682	ACCACAUU	CUGAUGA	X	GAA	AGAUGGUG	CACCAUCUC	AAUGUGGU
	2691	AGAAGGUU	CUGAUGA	X	GAA	ACCACAUU	AAUGUGGUC	AACCUUCU
	2697	GCACCUAG	CUGAUGA	X	GAA	AGGUUGAC	GUCAACCUU	CUAGGUGC
	2698	GGCACCUA	CUGAUGA	X	GAA	AAGGUUGA	UCAACCUUC	UAGGUGCC
30	2700	CAGGCACC	CUGAUGA	X	GAA	AGAAGGUU	AACCUUCUA	GGUGCCUG
	2710	UGGCUUGG	CUGAUGA	X	GAA	ACAGGCAC	GUGCCUGUA	CCAAGCCA
	2730	AUCACCAU	CUGAUGA	X	GAA	AGUGGCCC	GGGCCACUC	AUGGUGAU
	2739	AAUUCCAC	CUGAUGA	X	GAA	AUCACCAU	AUGGUGAUU	GUGGAAUU

	2747	AUUUGCAG	CUGAUGA	x	GAA	AUUCCACA	UGUGGAAUU	CUGCAAAU
	2748	AAUUUGCA	CUGAUGA	X	GAA	AAUUCCAC	GUGGAAUUC	UGCAAAUU
	2756	GGUUUCCA	CUGAUGA	X	GAA	AUUUGCAG	CUGCAAAUU	UGGAAACC
	2757	AGGUUUCC	CUGAUGA	X	GAA	AAUUUGCA	UGCAAAUUU	GGAAACCU
5	2768	GGUAAGUG	CUGAUGA	X	GAA	ACAGGUUU	AAACCUGUC	CACUUACC
	2773	CCUCAGGU	CUGAUGA	X	GAA	AGUGGACA	UGUCCACUU	ACCUGAGG
	2774	UCCUCAGG	CUGAUGA	X	GAA	AAGUGGAC	GUCCACUUA	CCUGAGGA
	2798	AGGGGACA	CUGAUGA	X	GAA	AUUCAUUU	AAAUGAAUU	UGUCCCCU
	2799	UAGGGGAC	CUGAUGA	X	GAA	AAUUCAUU	AAUGAAUUU	GUCCCCUA
10	2802	UUGUAGGG	CUGAUGA	X	GAA	ACAAAUUC	GAAUUUGUC	CCCUACAA
	2807	UGGUCUUG	CUGAUGA	X	GAA	AGGGGACA	UGUCCCCUA	CAAGACCA
	2828	CUUGACGG	CUGAUGA	X	GAA	AUCGUGCC	GGCACGAUU	CCGUCAAG
	2829	CCUUGACG	CUGAUGA	X	GAA	AAUCGUGC	GCACGAUUC	CGUCAAGG
	2833	UUUCCCUU	CUGAUGA	X	GAA	ACGGAAUC	GAUUCCGUC	AAGGGAAA
15	2846	CUCCAACG	CUGAUGA	X	GAA	AGUCUUUC	GAAAGACUA	CGUUGGAG
	2850	AUUGCUCC	CUGAUGA	X	GAA	ACGUAGUC	GACUACGUU	GGAGCAAU
	2859	UCCACAGG	CUGAUGA	X	GAA	AUUGCUCC	GGAGCAAUC	CCUGUGGA
	2869	CCGUUUCA	CUGAUGA	X	GAA	AUCCACAG	CUGUGGAUC	UGAAACGG
	2882	UGCUGUCC	CUGAUGA	X	GAA	AGCGCCGU	ACGGCGCUU	GGACAGCA
20	2892	CUACUGGU	CUGAUGA	X	GAA	AUGCUGUC	GACAGCAUC	ACCAGUAG
	2899	GCUCUGGC	CUGAUGA	X	GAA	ACUGGUGA	UCACCAGUA	GCCAGAGC
	2909	AGCUGGCU	CUGAUGA	X	GAA	AGCUCUGG	CCAGAGCUC	AGCCAGCU
	2918	CAAAUCCA	CUGAUGA	X	GAA	AGCUGGCU	AGCCAGCUC	UGGAUUUG
	2924	CCUCCACA	CUGAUGA	X	GAA	AUCCAGAG	CUCUGGAUU	UGUGGAGG
25	2925	UCCUCCAC	CUGAUGA	X	GAA	AAUCCAGA	UCUGGAUUU	GUGGAGGA
	2939	CACUGAGG	CUGAUGA	X	GAA	ACUUCUCC	GGAGAAGUC	CCUCAGUG
	2943	ACAUCACU	CUGAUGA	X	GAA	AGGGACUU	AAGUCCCUC	AGUGAUGU
	2952	UCUUCUUC	CUGAUGA	X	GAA	ACAUCACU	AGUGAUGUA	GAAGAAGA
	2968	AUCUUCAG	CUGAUGA	X	GAA	AGCUUCCU	AGGAAGCUC	CUGAAGAU
30	2977	CUUAUACA	CUGAUGA	X	GAA	AUCUUCAG	CUGAAGAUC	UGUAUAAG
	2981	AGUCCUUA	CUGAUGA	X	GAA	ACAGAUCU	AGAUCUGUA	UAAGGACU
	2983	GAAGUCCU	CUGAUGA	X	GAA	AUACAGAU	AUCUGUAUA	AGGACUUC
	2990	AGGUCAGG	CUGAUGA	X	GAA	AGUCCUUA	UAAGGACUU	CCUGACCU

	2991	AAGGUCAG	CUGAUGA	X	GAA	AAGUCCUU	AAGGACUUC	CUGACCUU
	2999	GAUGCUCC	CUGAUGA	X	GAA	AGGUCAGG	CCUGACCUU	GGAGCAUC
	3007	ACAGAUGA	CUGAUGA	x	GAA	AUGCUCCA	UGGAGCAUC	UCAUCUGU
	3009	UAACAGAU	CUGAUGA	x	GAA	AGAUGCUC	GAGCAUCUC	AUCUGUUA
5	3012	CUGUAACA	CUGAUGA	X	GAA	AUGAGAUG	CAUCUCAUC	UGUUACAG
	3016	GAAGCUGU	CUGAUGA	X	GAA	ACAGAUGA	UCAUCUGUU	ACAGCUUC
	3017	GGAAGCUG	CUGAUGA	x	GAA	AACAGAUG	CAUCUGUUA	CAGCUUCC
	3023	CCACUUGG	CUGAUGA	X	GAA	AGCUGUAA	UUACAGCUU	CCAAGUGG
	3024	GCCACUUG	CUGAUGA	X	GAA	AAGCUGUA	UACAGCUUC	CAAGUGGC
10	3034	CAUGCCCU	CUGAUGA	X	GAA	AGCCACUU	AAGUGGCUA	AGGGCAUG
	3047	AUGCCAAG	CUGAUGA	X	GAA	ACUCCAUG	CAUGGAGUU	CUUGGCAU
	3048	GAUGCCAA	CUGAUGA	X	GAA	AACUCCAU	AUGGAGUUC	UUGGCAUC
	3050	GCGAUGCC	CUGAUGA	X	GAA	AGAACUCC	GGAGUUCUU	GGCAUCGC
	3056	ACUUUCGC	CUGAUGA	X	GAA	AUGCCAAG	CUUGGCAUC	GCGAAAGU
15	3067	CCUGUGGA	CUGAUGA	X	GAA	ACACUUUC	GAAAGUGUA	UCCACAGG
	3069	UCCCUGUG	CUGAUGA	x	GAA	AUACACUU	AAGUGUAUC	CACAGGGA
	3094	UAAGAGGA	CUGAUGA	X	GAA	AUUUCGUG	CACGAAAUA	UCCUCUUA
	3096	GAUAAGAG	CUGAUGA	X	GAA	AUAUUUCG	CGAAAUAUC	CUCUUAUC
	3099	UCCGAUAA	CUGAUGA	X	GAA	AGGAUAUU	AAUAUCCUC	UUAUCGGA
20	3101	UCUCCGAU	CUGAUGA	X	GAA	AGAGGAUA	UAUCCUCUU	AUCGGAGA
	3102	UUCUCCGA	CUGAUGA	X	GAA	AAGAGGAU	AUCCUCUUA	UCGGAGAA
	3104	ucuucucc	CUGAUGA	X	GAA	AUAAGAGG	CCUCUUAUC	GGAGAAGA
	3120	CAGAUUUU	CUGAUGA	X	GAA	ACCACGUU	AACGUGGUU	AAAAUCUG
	3121	ACAGAUUU	CUGAUGA	X	GAA	AACCACGU	ACGUGGUUA	AAAUCUGU
25	3126	AAGUCACA	CUGAUGA	X	GAA	AUUUUAAC	GUUAAAAUC	UGUGACUU
	3134	CCAAGCCA	CUGAUGA	X	GAA	AGUCACAG	CUGUGACUU	UGGCUUGG
	3135	GCCAAGCC	CUGAUGA	X	GAA	AAGUCACA	UGUGACUUU	GGCUUGGC
	3140	CCCGGGCC	CUGAUGA	X	GAA	AGCCAAAG	CUUUGGCUU	GGCCCGGG
	3151	UUUAUAAA	CUGAUGA	X	GAA	AUCCCGGG	CCCGGGAUA	UUUAUAAA
30	3153	UCUUUAUA	CUGAUGA	X	GAA	AUAUCCCG	CGGGAUAUU	UAUAAAGA
	3154	AUCUUUAU	CUGAUGA	X	GAA	AAUAUCCC	GGGAUAUUU	AUAAAGAU
	3155	GAUCUUUA	CUGAUGA	X	GAA	AAAUAUCC	GGAUAUUUA	UAAAGAUC
	3157	UGGAUCUU	CUGAUGA	X	GAA	AUAAAUAU	AUAUUUAUA	AAGAUCCA

	3163	AUAAUCUG	CUGAUGA	Х	GAA	AUCUUUAU	AUAAAGAUC	CAGAUUAU
	3169	UCUGACAU	CUGAUGA	X	GAA	AUCUGGAU	AUCCAGAUU	AUGUCAGA
	3170	UUCUGACA	CUGAUGA	X	GAA	AAUCUGGA	UCCAGAUUA	UGUCAGAA
	3174	ccuuuucu	CUGAUGA	X	GAA	ACAUAAUC	GAUUAUGUC	AGAAAAGG
5	3190	AGGGAGGC	CUGAUGA	X	GAA	AGCAUCUC	GAGAUGCUC	GCCUCCCU
	3195	UUCAAAGG	CUGAUGA	x	GAA	AGGCGAGC	GCUCGCCUC	CCUUUGAA
	3199	CCAUUUCA	CUGAUGA	X	GAA	AGGGAGGC	GCCUCCCUU	UGAAAUGG
	3200	UCCAUUUC	CUGAUGA	X	GAA	AAGGGAGG	CCUCCCUUU	GAAAUGGA
	3225	CUGUCAAA	CUGAUGA	X	GAA	AUUGUUUC	GAAACAAUU	UUUGACAG
10	3226	UCUGUCAA	CUGAUGA	X	GAA	AAUUGUUU	AAACAAUUU	UUGACAGA
	3227	CUCUGUCA	CUGAUGA	X	GAA	AAAUUGUU	AACAAUUUU	UGACAGAG
	3228	ACUCUGUC	CUGAUGA	X	GAA	AAAAUUGU	ACAAUUUUU	GACAGAGU
	3239	GGAUUGUG	CUGAUGA	X	GAA	ACACUCUG	CAGAGUGUA	CACAAUCC
	3246	UCACUCUG	CUGAUGA	X	GAA	AUUGUGUA	UACACAAUC	CAGAGUGA
15	3258	AAAGACCA	CUGAUGA	X	GAA	ACGUCACU	AGUGACGUC	UGGUCUUU
	3263	CACCAAAA	CUGAUGA	X	GAA	ACCAGACG	CGUCUGGUC	UUUUGGUG
	3265	AACACCAA	CUGAUGA	X	GAA	AGACCAGA	UCUGGUCUU	UUGGUGUU
	3266	AAACACCA	CUGAUGA	X	GAA	AAGACCAG	CUGGUCUUU	UGGUGUUU
	3267	AAAACACC	CUGAUGA	X	GAA	AAAGACCA	UGGUCUUUU	GGUGUUUU
20	3273	CACAGCAA	CUGAUGA	X	GAA	ACACCAAA	UUUGGUGUU	UUGCUGUG
	3274	CCACAGCA	CUGAUGA	X	GAA	AACACCAA	UUGGUGUUU	UGCUGUGG
	3275	CCCACAGC	CUGAUGA	X	GAA	AAACACCA	UGGUGUUUU	GCUGUGGG
	3288	AAGGAAAA	CUGAUGA	X	GAA	AUUUCCCA	UGGGAAAUA	טטטטככטט
	3290	CUAAGGAA	CUGAUGA	X	GAA	AUAUUUCC	GGAAAUAUU	UUCCUUAG
25	3291	CCUAAGGA	CUGAUGA	X	GAA	AAUAUUUC	GAAAUAUUU	UCCUUAGG
	3292	ACCUAAGG	CUGAUGA	X	GAA	UUUAUAAA	UUUUAUAAA	CCUUAGGU
	3293	CACCUAAG	CUGAUGA	X	GAA	UUAUAAAA	AAUAUUUUC	CUUAGGUG
	3296	AAGCACCU	CUGAUGA	X	GAA	AGGAAAAU	AUUUUCCUU	AGGUGCUU
	3297	GAAGCACC	CUGAUGA	X	GAA	AAGGAAAA	UUUUCCUUA	GGUGCUUC
30	3304	AUAUGGAG	CUGAUGA	X	GAA	AGCACCUA	UAGGUGCUU	CUCCAUAU
	3305	GAUAUGGA	CUGAUGA	X	GAA	AAGCACCU	AGGUGCUUC	UCCAUAUC
	3307	AGGAUAUG	CUGAUGA	X	GAA	AGAAGCAC	GUGCUUCUC	CAUAUCCU
	3311	CCCCAGGA	CUGAUGA	X	GAA	AUGGAGAA	UUCUCCAUA	UCCUGGG

	3313	UACCCCAG	CUGAUGA	X	GAA	AUAUGGAG	CUCCAUAUC	CUGGGGUA
	3321	UCAAUCUU	CUGAUGA	X	GAA	ACCCCAGG	CCUGGGGUA	AAGAUUGA
	3327	UCUUCAUC	CUGAUGA	X	GAA	AUCUUUAC	GUAAAGAUU	GAUGAAGA
	3338	GCCUACAA	CUGAUGA	X	GAA	AUUCUUCA	UGAAGAAUU	UUGUAGGC
5	3339	CGCCUACA	CUGAUGA	X	GAA	AAUUCUUC	GAAGAAUUU	UGUAGGCG
	3340	UCGCCUAC	CUGAUGA	X	GAA	AAAUUCUU	AAGAAUUUU	GUAGGCGA
	3343	CAAUCGCC	CUGAUGA	X	GAA	ACAAAAUU	AAUUUUGUA	GGCGAUUG
	3350	CUUCUUUC	CUGAUGA	X	GAA	AUCGCCUA	UAGGCGAUU	GAAAGAAG
	3364	CCUCAUUC	CUGAUGA	X	GAA	AGUUCCUU	AAGGAACUA	GAAUGAGG
10	3382	UGUAGUAU	CUGAUGA	X	GAA	AUCAGGGG	CCCCUGAUU	AUACUACA
	3383	GUGUAGUA	CUGAUGA	X	GAA	AAUCAGGG	CCCUGAUUA	UACUACAC
	3385	UGGUGUAG	CUGAUGA	x	GAA	AUAAUCAG	CUGAUUAUA	CUACACCA
	3388	UUCUGGUG	CUGAUGA	X	GAA	AGUAUAAU	AUUAUACUA	CACCAGAA
	3401	UGGUCUGG	CUGAUGA	X	GAA	ACAUUUCU	AGAAAUGUA	CCAGACCA
15	3439	GGGUCUCU	CUGAUGA	X	GAA	ACUGGGCU	AGCCCAGUC	AGAGACCC
	3452	ACUCUGAA	CUGAUGA	X	GAA	ACGUGGGU	ACCCACGUU	UUCAGAGU
	3453	AACUCUGA	CUGAUGA	X	GAA	AACGUGGG	CCCACGUUU	UCAGAGUU
	3454	CAACUCUG	CUGAUGA	X	GAA	AAACGUGG	CCACGUUUU	CAGAGUUG
	3455	CCAACUCU	CUGAUGA	X	GAA	AAAACGUG	CACGUUUUC	AGAGUUGG
20	3461	GUUCCACC	CUGAUGA	X	GAA	ACUCUGAA	UUCAGAGUU	GGUGGAAC
	3472	AUUUCCCA	CUGAUGA	X	GAA	AUGUUCCA	UGGAACAUU	UGGGAAAU
	3473	GAUUUCCC	CUGAUGA	X	GAA	AAUGUUCC	GGAACAUUU	GGGAAAUC
	3481	UUGCAAGA	CUGAUGA	X	GAA	AUUUCCCA	UGGGAAAUC	UCUUGCAA
	3483	GCUUGCAA	CUGAUGA	X	GAA	AGAUUUCC	GGAAAUCUC	UUGCAAGO
25	3485	UAGCUUGC	CUGAUGA	X	GAA	AGAGAUUU	AAAUCUCUU	GCAAGCUA
	3493	CUGAGCAU	CUGAUGA	X	GAA	AGCUUGCA	UGCAAGCUA	AUGCUCAG
	3499	AUCCUGCU	CUGAUGA	X	GAA	AGCAUUAG	CUAAUGCUC	AGCAGGAU
	3518	GAACAAUG	CUGAUGA	X	GAA	AGUCUUUG	CAAAGACUA	CAUUGUUC
	3522	GGAAGAAC	CUGAUGA	X	GAA	AUGUAGUC	GACUACAUU	GUUCUUCO
30	3525	AUCGGAAG	CUGAUGA	X	GAA	ACAAUGUA	UACAUUGUU	CUUCCGAU
	3526	UAUCGGAA	CUGAUGA	X	GAA	AACAAUGU	ACAUUGUUC	UUCCGAUA
	3528	GAUAUCGG	CUGAUGA	X	GAA	AGAACAAU	AUUGUUCUU	CCGAUAU
	3529	UGAUAUCG	CUGAUGA	X	GAA	AAGAACAA	UUGUUCUUC	CGAUAUCA

	3534	GUCUCUGA	CUGAUGA	X	GAA	AUCGGAAG	CUUCCGAUA	UCAGAGAC
	3536	AAGUCUCU	CUGAUGA	X	GAA	AUAUCGGA	UCCGAUAUC	AGAGACUU
	3544	CAUGCUCA	CUGAUGA	X	GAA	AGUCUCUG	CAGAGACUU	UGAGCAUG
	3545	CCAUGCUC	CUGAUGA	X	GAA	AAGUCUCU	AGAGACUUU	GAGCAUGG
5	3562	GAGUCCAG	CUGAUGA	X	GAA	AUCCUCUU	AAGAGGAUU	CUGGACUC
	3563	AGAGUCCA	CUGAUGA	X	GAA	AAUCCUCU	AGAGGAUUC	UGGACUCU
	3570	GGCAGAGA	CUGAUGA	X	GAA	AGUCCAGA	UCUGGACUC	UCUCUGCC
	3572	UAGGCAGA	CUGAUGA	X	GAA	AGAGUCCA	UGGACUCUC	UCUGCCUA
	3574	GGUAGGCA	CUGAUGA	X	GAA	AGAGAGUC	GACUCUCUC	UGCCUACC
10	3580	AGGUGAGG	CUGAUGA	X	GAA	AGGCAGAG	CUCUGCCUA	CCUCACCU
	3584	AAACAGGU	CUGAUGA	X	GAA	AGGUAGGC	GCCUACCUC	ACCUGUUU
	3591	AUACAGGA	CUGAUGA	X	GAA	ACAGGUGA	UCACCUGUU	UCCUGUAU
	3592	CAUACAGG	CUGAUGA	X	GAA	AACAGGUG	CACCUGUUU	CCUGUAUG
	3593	CCAUACAG	CUGAUGA	X	GAA	AAACAGGU	ACCUGUUUC	CUGUAUGG
15	3598	CUCCUCCA	CUGAUGA	X	GAA	ACAGGAAA	UUUCCUGUA	UGGAGGAG
	3615	GGGUCACA	CUGAUGA	X	GAA	ACUUCCUC	GAGGAAGUA	UGUGACCC
	3629	CAUAAUGG	CUGAUGA	X	GAA	AUUUGGGG	CCCCAAAUU	CCAUUAUG
	3630	UCAUAAUG	CUGAUGA	X	GAA	AAUUUGGG	CCCAAAUUC	CAUUAUGA
	3634	GUUGUCAU	CUGAUGA	X	GAA	AUGGAAUU	AAUUCCAUU	AUGACAAC
20	3635	UGUUGUCA	CUGAUGA	X	GAA	AAUGGAAU	AUUCCAUUA	UGACAACA
	3654	UACUGACU	CUGAUGA	X	GAA	AUUCCUGC	GCAGGAAUC	AGUCAGUA
	3658	CAGAUACU	CUGAUGA	X	GAA	ACUGAUUC	GAAUCAGUC	AGUAUCUG
	3662	UCUGCAGA	CUGAUGA	X	GAA	ACUGACUG	CAGUCAGUA	UCUGCAGA
	3664	GUUCUGCA	CUGAUGA	X	GAA	AUACUGAC	GUCAGUAUC	UGCAGAAC
25	3676	CUUUCGCU	CUGAUGA	X	GAA	ACUGUUCU	AGAACAGUA	AGCGAAAG
	3702	AAUGUUUU	CUGAUGA	X	GAA	ACACUCAC	GUGAGUGUA	AAAACAUU
	3710	UAUCUUCA	CUGAUGA	X	GAA	AUGUUUUU	AAAAACAUU	UGAAGAUA
	3711	AUAUCUUC	CUGAUGA	X	GAA	AAUGUUUU	AAAACAUUU	GAAGAUAU
	3718	UAACGGGA	CUGAUGA	X	GAA	AUCUUCAA	UUGAAGAUA	UCCCGUUA
30	3720	UCUAACGG	CUGAUGA	X	GAA	AUAUCUUC	GAAGAUAUC	CCGUUAGA
	3725	GUUCUUCU	CUGAUGA	X	GAA	ACGGGAUA	UAUCCCGUU	AGAAGAAC
	3726	GGUUCUUC	CUGAUGA	X	GAA	AACGGGAU	AUCCCGUUA	GAAGAACC
	3741	AUUACUUU	CUGAUGA	X	GAA	ACUUCUGG	CCAGAAGUA	AAAGUAAU

	3747	UCUGGGAU	CUGAUGA	X	GAA	ACUUUUAC	GUAAAAGUA	AUCCCAGA
	3750	UCAUCUGG	CUGAUGA	X	GAA	AUUACUUU	AAAGUAAUC	CCAGAUGA
	3778	AAGAACCA	CUGAUGA	X	GAA	ACCACUGU	ACAGUGGUA	UGGUUCUU
	3783	GAGGCAAG	CUGAUGA	X	GAA	ACCAUACC	GGUAUGGUU	CUUGCCUC
5	3784	UGAGGCAA	CUGAUGA	x	GAA	AACCAUAC	GUAUGGUUC	UUGCCUCA
	3786	UCUGAGGC	CUGAUGA	x	GAA	AGAACCAU	AUGGUUCUU	GCCUCAGA
	3791	GCUCUUCU	CUGAUGA	X	GAA	AGGCAAGA	UCUUGCCUC	AGAAGAGC
	3808	GUCUUCCA	CUGAUGA	X	GAA	AGUUUUCA	UGAAAACUU	UGGAAGAC
	3809	UGUCUUCC	CUGAUGA	X	GAA	AAGUUUUC	GAAAACUUU	GGAAGACA
10	3827	AUGGAGAU	CUGAUGA	X	GAA	AUUUGGUU	AACCAAAUU	AUCUCCAU
	3828	GAUGGAGA	CUGAUGA	X	GAA	AAUUUGGU	ACCAAAUUA	UCUCCAUC
	3830	AAGAUGGA	CUGAUGA	X	GAA	AUAAUUUG	CAAAUUAUC	UCCAUCUU
	3832	AAAAGAUG	CUGAUGA	X	GAA	AGAUAAUU	AAUUAUCUC	CAUCUUUU
	3836	CACCAAAA	CUGAUGA	X	GAA	AUGGAGAU	AUCUCCAUC	UUUUGGUG
15	3838	UCCACCAA	CUGAUGA	X	GAA	AGAUGGAG	CUCCAUCUU	UUGGUGGA
	3839	UUCCACCA	CUGAUGA	X	GAA	AAGAUGGA	UCCAUCUUU	UGGUGGAA
	3840	AUUCCACC	CUGAUGA	X	GAA	AAAGAUGG	CCAUCUUUU	GGUGGAAU
	3872	AUGCCACA	CUGAUGA	X	GAA	ACUCCCUG	CAGGGAGUC	UGUGGCAU
	3881	AGCCUUCA	CUGAUGA	X	GAA	AUGCCACA	UGUGGCAUC	UGAAGGCU
20	3890	UCUGGUUU	CUGAUGA	X	GAA	AGCCUUCA	UGAAGGCUC	AAACCAGA
	3908	CGGACUGG	CUGAUGA	X	GAA	AGCCGCUU	AAGCGGCUA	CCAGUCCG
	3914	GAUAUCCG	CUGAUGA	X	GAA	ACUGGUAG	CUACCAGUC	CGGAUAUC
	3920	CGGAGUGA	CUGAUGA	X	GAA	AUCCGGAC	GUCCGGAUA	UCACUCCG
	3922	AUCGGAGU	CUGAUGA	X	GAA	AUAUCCGG	CCGGAUAUC	ACUCCGAU
25	3926	UGUCAUCG	CUGAUGA	X	GAA	AGUGAUAU	AUAUCACUC	CGAUGACA
	3950	CACUGGAG	CUGAUGA	X	GAA	ACACGGUG	CACCGUGUA	CUCCAGUG
	3953	CCUCACUG	CUGAUGA	X	GAA	AGUACACG	CGUGUACUC	CAGUGAGG
	3972	AGCUUUAA	CUGAUGA	X	GAA	AGUUCUGC	GCAGAACUU	UUAAAGCU
	3973	CAGCUUUA	CUGAUGA	X	GAA	AAGUUCUG	CAGAACUUU	UAAAGCUG
30	3974	UCAGCUUU	CUGAUGA	X	GAA	AAAGUUCU	AGAACUUUU	AAAGCUGA
	3975	AUCAGCUU	CUGAUGA	X	GAA	AAAAGUUC	GAACUUUUA	AAGCUGAU
	3984	CCAAUCUC	CUGAUGA	. X	GAA	AUCAGCUU	AAGCUGAUA	GAGAUUGG
	3990	UGCACUCC	CUGAUGA	. X	GAA	AUCUCUAU	AUAGAGAUU	GGAGUGCA

	4006	GGCUGUGC	CUGAUGA	Λ	GAA	ACCGGUUU	AAACCGGUA	GCACAGCC
	4020	GGCUGGAG	CUGAUGA	X	GAA	AUCUGGGC	GCCCAGAUU	CUCCAGCO
	4021	AGGCUGGA	CUGAUGA	X	GAA	AAUCUGGG	CCCAGAUUC	UCCAGCCU
	4023	UCAGGCUG	CUGAUGA	X	GAA	AGAAUCUG	CAGAUUCUC	CAGCCUGA
5	4052	CAGGAGGA	CUGAUGA	X	GAA	AGCUCAGU	ACUGAGCUC	uccuccuc
	4054	AACAGGAG	CUGAUGA	X	GAA	AGAGCUCA	UGAGCUCUC	CUCCUGUU
	4057	UUAAACAG	CUGAUGA	X	GAA	AGGAGAGC	GCUCUCCUC	CUGUUUAA
	4062	UCCUUUUA	CUGAUGA	X	GAA	ACAGGAGG	CCUCCUGUU	UAAAAGGA
	4063	חחככחחחח	CUGAUGA	X	GAA	AACAGGAG	CUCCUGUUU	AAAAGGAA
10	4064	CUUCCUUU	CUGAUGA	X	GAA	AAACAGGA	UCCUGUUUA	AAAGGAAG
	4076	GGGGUGUG	CUGAUGA	X	GAA	AUGCUUCC	GGAAGCAUC	CACACCCC
	4089	AUGUCCGG	CUGAUGA	X	GAA	AGUUGGGG	CCCCAACUC	CCGGACAU
	4098	UCUCAUGU	CUGAUGA	X	GAA	AUGUCCGG	CCGGACAUC	ACAUGAGA
	4110	UCUGAGCA	CUGAUGA	X	GAA	ACCUCUCA	UGAGAGGUC	UGCUCAGA
15	4115	CAAAAUCU	CUGAUGA	X	GAA	AGCAGACC	GGUCUGCUC	AGAUUUUG
	4120	CACUUCAA	CUGAUGA	X	GAA	AUCUGAGC	GCUCAGAUU	UUGAAGUG
	4121	ACACUUCA	CUGAUGA	X	GAA	AAUCUGAG	CUCAGAUUU	UGAAGUGU
	4122	AACACUUC	CUGAUGA	X	GAA	AAAUCUGA	UCAGAUUUU	GAAGUGUU
	4130	GAAAGAAC	CUGAUGA	X	GAA	ACACUUCA	UGAAGUGUU	GUUCUUUC
20	4133	GUGGAAAG	CUGAUGA	X	GAA	ACAACACU	AGUGUUGUU	CUUUCCAC
	4134	GGUGGAAA	CUGAUGA	X	GAA	AACAACAC	GUGUUGUUC	UUUCCACO
	4136	CUGGUGGA	CUGAUGA	X	GAA	AGAACAAC	GUUGUUCUU	UCCACCAG
	4137	GCUGGUGG	CUGAUGA	X	GAA	AAGAACAA	UUGUUCUUU	CCACCAGO
	4138	UGCUGGUG	CUGAUGA	X	GAA	AAAGAACA	UGUUCUUUC	CACCAGCA
25	4153	AAUGCGGC	CUGAUGA	X	GAA	ACUUCCUG	CAGGAAGUA	GCCGCAUU
	4161	GAAAAUCA	CUGAUGA	X	GAA	AUGCGGCU	AGCCGCAUU	UGAUUUUC
	4162	UGAAAAUC	CUGAUGA	X	GAA	AAUGCGGC	GCCGCAUUU	GAUUUUCA
	4166	GAAAUGAA	CUGAUGA	X	GAA	AUCAAAUG	CAUUUGAUU	UUCAUUUC
	4167	CGAAAUGA	CUGAUGA	X	GAA	AAUCAAAU	AUUUGAUUU	UCAUUUCG
30	4168	UCGAAAUG	CUGAUGA	X	GAA	AAAUCAAA	UUUGAUUUU	CAUUUCGA
	4169	GUCGAAAU	CUGAUGA	X	GAA	AAAAUCAA	UUGAUUUUC	AUUUCGAC
	4172	GUUGUCGA	CUGAUGA	X	GAA	AUGAAAAU	AUUUUCAUU	UCGACAAC
	4173	UGUUGUCG	CUGAUGA	X	GAA	AAUGAAAA	ппппсаппп	CGACAACA

117

	4174	CUGUUGUC	CUGAUGA	X	GAA	AAAUGAAA	UUUCAUUUC	GACAACAG
	4194	UGCAGUCC	CUGAUGA	X	GAA	AGGUCCUU	AAGGACCUC	GGACUGCA
	4214	GCCUAGAA	CUGAUGA	x	GAA	AGCUGGCU	AGCCAGCUC	UUCUAGGC
	4216	AAGCCUAG	CUGAUGA	X	GAA	AGAGCUGG	CCAGCUCUU	CUAGGCUU
5	4217	CAAGCCUA	CUGAUGA	x	GAA	AAGAGCUG	CAGCUCUUC	UAGGCUUG
	4219	CACAAGCC	CUGAUGA	х	GAA	AGAAGAGC	GCUCUUCUA	GGCUUGUG

Where "X" represents stem II region of a HH ribozyme (Hertel et al., 1992 Nucleic Acids Res. 20 3252). The length of stem II may be ≥ 2 base-pairs.

Table V: Human KDR VEGF Receptor-Hairpin Ribozyme and Substrate Sequences

PCT/US96/17480

CUUGGAGC

ACUUCCU GAC

GCUCCAAG AGAA GGAAGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

2993

WO 97/15662

119

CACUUACC CUGGAUUU GAACUCCC UVAUGAUG GAGACCG GCU GAACCUAG GCCUUNGG CACACCU GUU UGCAAGAA CUAGAGCG CAUGUGGU AUUGGCA GUU GGAGGAAG CCAAGCU GUC UCAGUGAC UUGUACAA CACUGAGC CUACGUUU GCC UCUGCCAA UUGCUCAA CACAGUCC AGAAUCA GAC GACAAGUA GCU GAU gcc GAU GAAACCU GUC UGUGUCA GCU GCAGACA GAU UAUGUCU GCC UCAGGCA GCU GGAUCCA GAU ACAUGCA GCC GUC CUCCACA AACGACU UCAGCCA UGAAGCA GCCCACA GCUCACA GUGAGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA UACUUGUC AGAA GAUUCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUGGAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGAGUUC AGAA GGAUCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CAUCAUAA AGAA GUCGUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CUAGGUUC AGAA GGUCUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CCAAAGGC AGAA GCUUCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGUAAGUG AGAA GGUUUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AAAUCCAG AGAA GGCUGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUCUGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUGGGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA UUCUUGCA AGAA GGUGUG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GACAUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGACUGUG AGAA GCCUGA ACCAGAGAAACACGCUGUGGGGAACAUUACCUGGUA CUUCCUCC AGAA GCCAAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GACACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCAUGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCUUGG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA ACCACAUG AGAA AGAA UUGUACAA AGAA UUGGCAGA AGAA UUGAGCAA AGAA CGCUCUAG AGAA GCUCAGUG AGAA AAACGUAG AGAA GUCACUGA 2418 1918 1974 2084 2453 2492 2547 2765 2914 1376 1569 1717 1760 1797 1967 2021 1413 1673 10 15 വ

GAGGUCU GCU CAGAUUUU

GACCUC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA

AAAAUCUG AGAA

4111

4059

ACUUCAAA AGAA

4116

4195

GAGCAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

UCCCUGCA AGAA GAGGUC ACCAGAGAACACACGUUGUGGGAACAUUACCUGGUA

GAU UUUGAAGU

CUGCUCA

GAC UGCAGGGA

GACCUCG

UGUUACA GCU UCCAAGUG GAU UAUACUAC GCU GGCACGGG UCUCUCU GCC UACCUCAC CUCACCU GUU UCCUGUAU AGAGCCG GCC UGUGAGUG GAU GACAACCA GAU UAUGUCAG UGUACCA GAC CAUGCUGG GGACAGUG GAU GACACAGA CAGAUUCU GAU UCUCCAGO UUCUCCA GCC UGACACGG UCCUCCU GUU UAAAAGGA CGGAUAUC GNC GAC UAGCACA GCC CUGGACU AAUCCCA GCUACCA AGAUCCA ACAACCA UCACUCC CAGCCCA GGCCCCU GUAACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUCCAG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GAGAGA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA AUACAGGA AGAA GGUGAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CACUCACA AGAA GGCUCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGAUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGUUGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAUAUCCG AGAA GGUAGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA GGUACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAGUGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AGAAUCUG AGAA GUGCUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGCUG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CCGUGUCA AGAA GGAGAA ACCAGAGAAACACACGUUGUGGGAACAUUACCUGGUA GGAGGA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGAUCU 225555 AGAA UCCUUUUA AGAA CACUUGGA AGAA SUAGUAUA AGAA CCAGCAUG AGAA CCCGUGCC AGAA GUGAGGUA AGAA AGAA UCUGUGUC AGAA AGAA CUGACAUA AGAA uggungnc CACUGUCC GCUGGAGA 3019 3418 3575 3588 3165 3378 3404 3689 3753 3764 3911 4011 4016 4025 3927 10 15 ហ

PCT/US96/17480

GGAGCCA GCU CUUCUAGG CCUAGAAG AGAA GGCUCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

4210

122

Table VI: Mouse flk-1 VEGF Receptor-Hammerhead Ribozyme and Substrate Sequence

	nt. HH Ribozyme			ne	Sequ	ience	Subst	rate
	Posi							
5	tion	ı						
	13	CCGUACCC	CUGAUGA	X	GAA	AUUCGCCC	GGGCGAAUU	GGGUACGG
	18	GGGUCCCG	CUGAUGA	X	GAA	ACCCAAUU	AAUUGGGUA	CGGGACCC
	31	UCGACCUC	CUGAUGA	X	GAA	AGGGGGGU	ACCCCCCUC	GAGGUCGA
	37	AUACCGUC	CUGAUGA	X	GAA	ACCUCGAG	CUCGAGGUC	GACGGUAU
10	44	CUUAUCGA	CUGAUGA	X	GAA	ACCGUCGA	UCGACGGUA	UCGAUAAG
	46	AGCUUAUC	CUGAUGA	X	GAA	AUACCGUC	GACGGUAUC	GAUAAGCU
	50	AUCAAGCU	CUGAUGA	X	GAA	AUCGAUAC	GUAUCGAUA	AGCUUGAU
	55	UCGAUAUC	CUGAUGA	X	GAA	AGCUUAUC	GAUAAGCUU	GAUAUCGA
	59	GAAUUCGA	CUGAUGA	X	GAA	AUCAAGCU	AGCUUGAUA	UCGAAUUC
15	61	CCGAAUUC	CUGAUGA	X	GAA	AUAUCAAG	CUUGAUAUC	GAAUUCGG
	66	UGGGCCCG	CUGAUGA	X	GAA	AUUCGAUA	UAUCGAAUU	CGGGCCCA
	67	CUGGGCCC	CUGAUGA	X	GAA	AAUUCGAU	AUCGAAUUC	GGGCCCAG
	83	GGCUGCGG	CUGAUGA	X	GAA	ACACAGUC	GACUGUGUC	CCGCAGCC
	97	AGCCAGGU	CUGAUGA	X	GAA	AUCCCGGC	GCCGGGAUA	ACCUGGCU
20	114	GUCCGCGG	CUGAUGA	X	GAA	AUCGGGUC	GACCCGAUU	CCGCGGAC
	115	UGUCCGCG	CUGAUGA	X	GAA	AAUCGGGU	ACCCGAUUC	CGCGGACA
	169	ACCGGGGA	CUGAUGA	X	GAA	AGCGCGGG	CCCGCGCUC	UCCCCGGU
	171	AGACCGGG	CUGAUGA	X	GAA	AGAGCGCG	CGCGCUCUC	CCCGGUCU
	178	CAGCGCAA	CUGAUGA	X	GAA	ACCGGGGA	UCCCCGGUC	UUGCGCUG
25	180	CGCAGCGC	CUGAUGA	X	GAA	AGACCGGG	CCCGGUCUU	GCGCUGCG
	197	AGAGGCGG	CUGAUGA	X	GAA	AUGGCCCC	GGGGCCAUA	CCGCCUCU
	204	AAGUCACA	CUGAUGA	X	GAA	AGGCGGUA	UACCGCCUC	UGUGACUU
	212	CCGCAAAG	CUGAUGA	X	GAA	AGUCACAG	CUGUGACUU	CUUUGCGG
	213	CCCGCAAA	CUGAUGA	X	GAA	AAGUCACA	UGUGACUUC	UUUGCGGG
30	215	GGCCCGCA	CUGAUGA	X	GAA	AGAAGUCA	UGACUUCUU	UGCGGGCC

PCT/US96/17480

WO 97/15662

	216	UGGCCCGC	CUGAUGA	X	GAA	AAGAAGUC	GACUUCUUU	GCGGGCCA
	241	CAGGCACA	CUGAUGA	X	GAA	ACUCCUUC	GAAGGAGUC	UGUGCCUG
	262	UGGGCACA	CUGAUGA	x	GAA	AGCCCAGU	ACUGGGCUC	UGUGCCCA
	306	GCGACAGC	CUGAUGA	X	GAA	AGCAGCGC	GCGCUGCUA	GCUGUCGC
5	312	CACAGAGC	CUGAUGA	X	GAA	ACAGCUAG	CUAGCUGUC	GCUCUGUG
	316	GAACCACA	CUGAUGA	X	GAA	AGCGACAG	CUGUCGCUC	UGUGGUUC
	323	CCACGCAG	CUGAUGA	X	GAA	ACCACAGA	ucugugguu	CUGCGUGG
	324	UCCACGCA	CUGAUGA	X	GAA	AACCACAG	CUGUGGUUC	UGCGUGGA
	347	AACCCACA	CUGAUGA	X	GAA	AGGCGGCU	AGCCGCCUC	UGUGGGUU
10	355	GCCAGUCA	CUGAUGA	X	GAA	ACCCACAG	CUGUGGGUU	UGACUGGC
	356	CGCCAGUC	CUGAUGA	X	GAA	AACCCACA	UGUGGGUUU	GACUGGCG
	367	AUGGAGAA	CUGAUGA	X	GAA	AUCGCCAG	CUGGCGAUU	UUCUCCAU
	368	GAUGGAGA	CUGAUGA	X	GAA	AAUCGCCA	UGGCGAUUU	UCUCCAUC
	369	GGAUGGAG	CUGAUGA	X	GAA	AAAUCGCC	GGCGAUUUU	CUCCAUCC
15	370	GGGAUGGA	CUGAUGA	X	GAA	AAAAUCGC	GCGAUUUUC	UCCAUCCC
	372	GGGGGAUG	CUGAUGA	X	GAA	AGAAAAUC	GAUUUUCUC	CAUCCCCC
	376	CUUGGGGG	CUGAUGA	X	GAA	AUGGAGAA	UUCUCCAUC	CCCCCAAG
	387	UGUGUGCU	CUGAUGA	X	GAA	AGCUUGGG	CCCAAGCUC	AGCACACA
	405	AUUGUCAG	CUGAUGA	X	GAA	AUGUCUUU	AAAGACAUA	CUGACAAU
20	414	UUUGCCAA	CUGAUGA	X	GAA	AUUGUCAG	CUGACAAUU	UUGGCAAA
	415	AUUUGCCA	CUGAUGA	X	GAA	AAUUGUCA	UGACAAUUU	UGGCAAAU
	416	UAUUUGCC	CUGAUGA	X	GAA	AAAUUGUC	GACAAUUUU	GGCAAAUA
	424	AAGGGUUG	CUGAUGA	X	GAA	AUUUGCCA	UGGCAAAUA	CAACCCUU
	432	GUAAUCUG	CUGAUGA	X	GAA	AGGGUUGU	ACAACCCUU	CAGAUUAC
25	433	AGUAAUCU	CUGAUGA	X	GAA	AAGGGUUG	CAACCCUUC	AGAUUACU
	438	CUGCAAGU	CUGAUGA	X	GAA	AUCUGAAG	CUUCAGAUU	ACUUGCAG
	439	CCUGCAAG	CUGAUGA	X	GAA	AAUCUGAA	UUCAGAUUA	CUUGCAGG
	442	UCCCCUGC	CUGAUGA	X	GAA	AGUAAUCU	AGAUUACUU	GCAGGGGA
	471	UUGGGCCA	CUGAUGA	X	GAA	AGCCAGUC	GACUGGCUU	UGGCCCAA
30	472	AUUGGGCC	CUGAUGA	X	GAA	AAGCCAGU	ACUGGCUUU	GGCCCAAU

	484	AUCACGCU	CUGAUGA	Х	GAA	AGCAUUGG	CCAAUGCUC	AGCGUGAU
	493	UUCCUCAG	CUGAUGA	X	GAA	AUCACGCU	AGCGUGAUU	CUGAGGAA
	494	UUUCCUCA	CUGAUGA	X	GAA	AAUCACGC	GCGUGAUUC	UGAGGAAA
	507	GUCACCAA	CUGAUGA	X	GAA	ACCCUUUC	GAAAGGGUA	UUGGUGAC
5	509	CAGUCACC	CUGAUGA	X	GAA	AUACCCUU	AAGGGUAUU	GGUGACUG
	538	GCAGAAGA	CUGAUGA	X	GAA	ACUGUCAC	GUGACAGUA	UCUUCUGC
	540	UUGCAGAA	CUGAUGA	X	GAA	AUACUGUC	GACAGUAUC	UUCUGCAA
	542	UUUUGCAG	CUGAUGA	X	GAA	AGAUACUG	CAGUAUCUU	CUGCAAAA
	54 3	GUUUUGCA	CUGAUGA	X	GAA	AAGAUACU	AGUAUCUUC	UGCAAAAC
10	555	GGAAUGGU	CUGAUGA	X	GAA	AGUGUUUU	AAAACACUC	ACCAUUCC
	561	ACCCUGGG	CUGAUGA	X	GAA	AUGGUGAG	CUCACCAUU	CCCAGGGU
	562	CACCCUGG	CUGAUGA	X	GAA	AAUGGUGA	UCACCAUUC	CCAGGGUG
	57 3	UCAUUUCC	CUGAUGA	X	GAA	ACCACCCU	AGGGUGGUU	GGAAAUGA
	583	GGCUCCAG	CUGAUGA	X	GAA	AUCAUUUC	GAAAUGAUA	CUGGAGCC
15	59 3	AGCACUUG	CUGAUGA	X	GAA	AGGCUCCA	UGGAGCCUA	CAAGUGCU
	602	CCCGGUAC	CUGAUGA	X	GAA	AGCACUUG	CAAGUGCUC	GUACCGGG
	605	CGUCCCGG	CUGAUGA	X	GAA	ACGAGCAC	GUGCUCGUA	CCGGGACG
	615	GCUAUGUC	CUGAUGA	X	GAA	ACGUCCCG	CGGGACGUC	GACAUAGC
	621	GUGGAGGC	CUGAUGA	X	GAA	AUGUCGAC	GUCGACAUA	GCCUCCAC
20	626	AAACAGUG	CUGAUGA	X	GAA	AGGCUAUG	CAUAGCCUC	CACUGUUU
	633	UAGACAUA	CUGAUGA	X	GAA	ACAGUGGA	UCCACUGUU	UAUGUCUA
	634	AUAGACAU	CUGAUGA	X	GAA	AACAGUGG	CCACUGUUU	AUGUCUAU
	635	CAUAGACA	CUGAUGA	X	GAA	AAACAGUG	CACUGUUUA	UGUCUAUG
	639	CGAACAUA	CUGAUGA	X	GAA	ACAUAAAC	GUUUAUGUC	UAUGUUCG
25	641	CUCGAACA	CUGAUGA	X	GAA	AGACAUAA	UUAUGUCUA	UGUUCGAG
	645	UAAUCUCG	CUGAUGA	X	GAA	ACAUAGAC	GUCUAUGUU	CGAGAUUA
	646	GUAAUCUC	CUGAUGA	X	GAA	AACAUAGA	UCUAUGUUC	GAGAUUAC
	652	UGAUCUGU	CUGAUGA	X	GAA	AUCUCGAA	UUCGAGAUU	ACAGAUCA
	653	GUGAUCUG	CUGAUGA	X	GAA	AAUCUCGA	UCGAGAUUA	CAGAUCAC
30	659	UGAAUGGU	CUGAUGA	X	GAA	AUCUGUAA	UUACAGAUC	ACCAUUCA

	665	AGGCGAUG	CUGAUGA	X	GAA	AUGGUGAU	AUCACCAUU	CAUCGCCU
	666	GAGGCGAU	CUGAUGA	X	GAA	AAUGGUGA	UCACCAUUC	AUCGCCUC
	669	ACAGAGGC	CUGAUGA	X	GAA	AUGAAUGG	CCAUUCAUC	GCCUCUGU
	674	CACUGACA	CUGAUGA	X	GAA	AGGCGAUG	CAUCGCCUC	UGUCAGUG
5	678	UGGUCACU	CUGAUGA	X	GAA	ACAGAGGC	GCCUCUGUC	AGUGACCA
	69 6	AUGUACAC	CUGAUGA	X	GAA	AUGCCAUG	CAUGGCAUC	GUGUACAU
	701	CGGUGAUG	CUGAUGA	X	GAA	ACACGAUG	CAUCGUGUA	CAUCACCG
	705	UUCUCGGU	CUGAUGA	x	GAA	AUGUACAC	GUGUACAUC	ACCGAGAA
	7 35	CGGCAGGG	CUGAUGA	x	GAA	AUCACCAC	GUGGUGAUC	CCCUGCCG
10	749	UUGAAAUC	CUGAUGA	X	GAA	ACCCUCGG	CCGAGGGUC	GAUUUCAA
	75 3	AGGUUUGA	CUGAUGA	X	GAA	AUCGACCC	GGGUCGAUU	UCAAACCU
	754	GAGGUUUG	CUGAUGA	X	GAA	AAUCGACC	GGUCGAUUU	CAAACCUC
	75 5	UGAGGUUU	CUGAUGA	X	GAA	AAAUCGAC	GUCGAUUUC	AAACCUCA
	76 2	GACACAUU	CUGAUGA	x	GAA	AGGUUUGA	UCAAACCUC	AAUGUGUC
15	77 0	CGCAAAGA	CUGAUGA	X	GAA	ACACAUUG	CAAUGUGUC	UCUUUGCG
	77 2	AGCGCAAA	CUGAUGA	X	GAA	AGACACAU	AUGUGUCUC	UUUGCGCU
	774	CUAGCGCA	CUGAUGA	X	GAA	AGAGACAC	GUGUCUCUU	UGCGCUAG
	77 5	CCUAGCGC	CUGAUGA	x	GAA	AAGAGACA	UGUCUCUUU	GCGCUAGG
	781	UGGAUACC	CUGAUGA	x	GAA	AGCGCAAA	UUUGCGCUA	GGUAUCCA
20	785	UUUCUGGA	CUGAUGA	X	GAA	ACCUAGCG	CGCUAGGUA	UCCAGAAA
	787	CUUUUCUG	CUGAUGA	X	GAA	AUACCUAG	CUAGGUAUC	CAGAAAAG
	800	CCGGAACA	CUGAUGA	X	GAA	AUCUCUUU	AAAGAGAUU	UGUUCCGG
	801	UCCGGAAC	CUGAUGA	X	GAA	AAUCUCUU	AAGAGAUUU	GUUCCGGA
	804	CCAUCCGG	CUGAUGA	X	GAA	ACAAAUCU	AGAUUUGUU	CCGGAUGG
25	805	UCCAUCCG	CUGAUGA	X	GAA	AACAAAUC	GAUUUGUUC	CGGAUGGA
	822	UCCCAGGA	CUGAUGA	X	GAA	AUUCUGUU	AACAGAAUU	UCCUGGGA
	823	GUCCCAGG	CUGAUGA	X	GAA	AAUUCUGU	ACAGAAUUU	CCUGGGAC
	824	UGUCCCAG	CUGAUGA	X	GAA	AAAUUCUG	CAGAAUUUC	CUGGGACA
	840	GUAAAGCC	CUGAUGA	X	GAA	AUCUCGCU	AGCGAGAUA	GGCUUUAC
30	845	GGAGAGUA	CUGAUGA	X	GAA	AGCCUAUC	GAUAGGCUU	UACUCUCC

	846	GGGAGAGU	CUGAUGA	X	GAA	AAGCCUAU	AUAGGCUUU	ACUCUCCC
	847	GGGGAGAG	CUGAUGA	X	GAA	AAAGCCUA	UAGGCUUUA	CUCUCCCC
	850	ACUGGGGA	CUGAUGA	X	GAA	AGUAAAGC	GCUUUACUC	UCCCCAGU
	852	UAACUGGG	CUGAUGA	X	GAA	AGAGUAAA	UUUACUCUC	CCCAGUUA
5	859	GAUCAUGU	CUGAUGA	X	GAA	ACUGGGGA	UCCCCAGUU	ACAUGAUC
	860	UGAUCAUG	CUGAUGA	X	GAA	AACUGGGG	CCCCAGUUA	CAUGAUCA
	867	GCAUAGCU	CUGAUGA	X	GAA	AUCAUGUA	UACAUGAUC	AGCUAUGC
	872	UGCCGGCA	CUGAUGA	X	GAA	AGCUGAUC	GAUCAGCUA	UGCCGGCA
	885	UCACAGAA	CUGAUGA	X	GAA	ACCAUGCC	GGCAUGGUC	UUCUGUGA
10 .	887	CCUCACAG	CUGAUGA	X	GAA	AGACCAUG	CAUGGUCUU	CUGUGAGG
	888	GCCUCACA	CUGAUGA	X	GAA	AAGACCAU	AUGGUCUUC	UGUGAGGC
	903	UCAUCAUU	CUGAUGA	X	GAA	AUCUUUGC	GCAAAGAUC	AAUGAUGA
	917	UAGACUGA	CUGAUGA	X	GAA	AGGUUUCA	UGAAACCUA	UCAGUCUA
	919	GAUAGACU	CUGAUGA	X	GAA	AUAGGUUU	AAACCUAUC	AGUCUAUC
15	923	ACAUGAUA	CUGAUGA	X	GAA	ACUGAUAG	CUAUCAGUC	UAUCAUGU
	925	GUACAUGA	CUGAUGA	X	GAA	AGACUGAU	AUCAGUCUA	UCAUGUAC
	927	AUGUACAU	CUGAUGA	X	GAA	AUAGACUG	CAGUCUAUC	AUGUACAU
	932	CAACUAUG	CUGAUGA	X	GAA	ACAUGAUA	UAUCAUGUA	CAUAGUUG
	9 36	ACCACAAC	CUGAUGA	X	GAA	AUGUACAU	AUGUACAUA	GUUGUGGU
20	939	ACAACCAC	CUGAUGA	X	GAA	ACUAUGUA	UACAUAGUU	GUGGUUGU
	945	UAUCCUAC	CUGAUGA	X	GAA	ACCACAAC	GUUGUGGUU	GUAGGAUA
	948	CUAUAUCC	CUGAUGA	X	GAA	ACAACCAC	GUGGUUGUA	GGAUAUAG
	953	AAAUCCUA	CUGAUGA	X	GAA	AUCCUACA	UGUAGGAUA	UAGGAUUU
	95 5	AUAAAUCC	CUGAUGA	X	GAA	AUAUCCUA	UAGGAUAUA	GGAUUUAU
2 5	960	ACAUCAUA	CUGAUGA	X	GAA	AUCCUAUA	UAUAGGAUU	UAUGAUGU
	961	CACAUCAU	CUGAUGA	X	GAA	AAUCCUAU	AUAGGAUUU	AUGAUGUG
	962	UCACAUCA	CUGAUGA	X	GAA	AAAUCCUA	UAGGAUUUA	UGAUGUGA
	972	GGGCUCAG	CUGAUGA	X	GAA	AUCACAUC	GAUGUGAUU	CUGAGCCC
	97 3	GGGGCUCA	CUGAUGA	X	GAA	AAUCACAU	AUGUGAUUC	UGAGCCCC
30	993	GAUAGCUC	CUGAUGA	X	GAA	AUUUCAUG	CAUGAAAUU	GAGCUAUC

	999	CCGGCAGA	CUGAUGA	x	GAA	AGCUCAAU	AUUGAGCUA	UCUGCCGG
	1001	CUCCGGCA	CUGAUGA	X	GAA	AUAGCUCA	UGAGCUAUC	UGCCGGAG
	1017	UUUAAGAC	CUGAUGA	X	GAA	AGUUUUUC	GAAAAACUU	GUCUUAAA
	1020	CAAUUUAA	CUGAUGA	X	GAA	ACAAGUUU	AAACUUGUC	UUAAAUUG
5	1022	UACAAUUU	CUGAUGA	X	GAA	AGACAAGU	ACUUGUCUU	AAAUUGUA
	1023	GUACAAUU	CUGAUGA	X	GAA	AAGACAAG	CUUGUCUUA	AAUUGUAC
	1027	CGCUGUAC	CUGAUGA	X	GAA	AUUUAAGA	UCUUAAAUU	GUACAGCG
	1030	UCUCGCUG	CUGAUGA	X	GAA	ACAAUUUA	UAAAUUGUA	CAGCGAGA
	1047	CCCACAUU	CUGAUGA	X	GAA	AGCUCUGU	ACAGAGCUC	AAUGUGGG
10	1059	GUGAAAUC	CUGAUGA	X	GAA	AGCCCCAC	GUGGGGCUU	GAUUUCAC
	1063	CCAGGUGA	CUGAUGA	X	GAA	AUCAAGCC	GGCUUGAUU	UCACCUGG
	1064	GCCAGGUG	CUGAUGA	X	GAA	AAUCAAGC	GCUUGAUUU	CACCUGGC
	1065	UGCCAGGU	CUGAUGA	X	GAA	AAAUCAAG	CUUGAUUUC	ACCUGGCA
	1076	AAGGUGGA	CUGAUGA	X	GAA	AGUGCCAG	CUGGCACUC	UCCACCUU
15	1078	UGAAGGUG	CUGAUGA	X	GAA	AGAGUGCC	GGCACUCUC	CACCUUCA
	1084	AGACUUUG	CUGAUGA	X	GAA	AGGUGGAG	CUCCACCUU	CAAAGUCU
	1085	GAGACUUU	CUGAUGA	X	GAA	AAGGUGGA	UCCACCUUC	AAAGUCUC
	1091	UAUGAUGA	CUGAUGA	X	GAA	ACUUUGAA	UUCAAAGUC	UCAUCAUA
	1093	CUUAUGAU	CUGAUGA	X	GAA	AGACUUUG	CAAAGUCUC	AUCAUAAG
20	1096	CUUCUUAU	CUGAUGA	X	GAA	AUGAGACU	AGUCUCAUC	AUAAGAAG
	1099	AAUCUUCU	CUGAUGA	X	GAA	AUGAUGAG	CUCAUCAUA	AGAAGAUU
	1107	CGGUUUAC	CUGAUGA	X	GAA	AUCUUCUU	AAGAAGAUU	GUAAACCG
	1110	UCCCGGUU	CUGAUGA	X	GAA	ACAAUCUU	AAGAUUGUA	AACCGGGA
	1130	UCCCAGGA	CUGAUGA	X	GAA	AGGGUUUC	GAAACCCUU	UCCUGGGA
25	1131	GUCCCAGG	CUGAUGA	X	GAA	AAGGGUUU	AAACCCUUU	CCUGGGAC
	1132	AGUCCCAG	CUGAUGA	X	GAA	AAAGGGUU	AACCCUUUC	CUGGGACU
	1154	UGCUCAAA	CUGAUGA	X	GAA	ACAUCUUC	GAAGAUGUU	UUUGAGCA
	1155	GUGCUCAA	CUGAUGA	X	GAA	AACAUCUU	AAGAUGUUU	UUGAGCAC
	1156	GGUGCUCA	CUGAUGA	X	GAA	AAACAUCU	AGAUGUUUU	UGAGCACC
30	1157	AGGUGCUC	CUGAUGA	X	GAA	AAAACAUC	GAUGUUUUU	GAGCACCU

	1166	CUAUUGUC	CUGAUGA	X	GAA	AGGUGCUC	GAGCACCUU GACAAUAG
	1173	ACACUUUC	CUGAUGA	X	GAA	AUUGUCAA	UUGACAAUA GAAAGUGU
	1205	CACAGGUG	CUGAUGA	X	GAA	AUUCCCCU	AGGGGAAUA CACCUGUG
	1215	CUGGACGC	CUGAUGA	X	GAA	ACACAGGU	ACCUGUGUA GCGUCCAG
5	1220	GUCCACUG	CUGAUGA	X	GAA	ACGCUACA	UGUAGCGUC CAGUGGAC
	1236	uuucucuu	CUGAUGA	X	GAA	AUCAUCCG	CGGAUGAUC AAGAGAAA
	1246	AAAUGUUC	CUGAUGA	X	GAA	AUUUCUCU	AGAGAAAUA GAACAUUU
	1253	CUCGGACA	CUGAUGA	X	GAA	AUGUUCUA	UAGAACAUU UGUCCGAG
	1254	ACUCGGAC	CUGAUGA	Х	GAA	AAUGUUCU	AGAACAUUU GUCCGAGU
10	1257	UGAACUCG	CUGAUGA	X	GAA	ACAAAUGU	ACAUUUGUC CGAGUUCA
	1263	UUUGUGUG	CUGAUGA	X	GAA	ACUCGGAC	GUCCGAGUU CACACAAA
	1264	CUUUGUGU	CUGAUGA	X	GAA	AACUCGGA	UCCGAGUUC ACACAAAG
	1276	AGCAAUAA	CUGAUGA	X	GAA	AGGCUUUG	CAAAGCCUU UUAUUGCU
	1277	AAGCAAUA	CUGAUGA	X	GAA	AAGGCUUU	AAAGCCUUU UAUUGCUU
15	1278	AAAGCAAU	CUGAUGA	X	GAA	AAAGGCUU	AAGCCUUUU AUUGCUUU
	1279	GAAAGCAA	CUGAUGA	X	GAA	AAAAGGCU	AGCCUUUUA UUGCUUUC
	1281	CCGAAAGC	CUGAUGA	X	GAA	AUAAAAGG	CCUUUUAUU GCUUUCGG
	1285	ACUACCGA	CUGAUGA	X	GAA	AGCAAUAA	UUAUUGCUU UCGGUAGU
	1286	CACUACCG	CUGAUGA	X	GAA	AAGCAAUA	UAUUGCUUU CGGUAGUG
20	1287	CCACUACC	CUGAUGA	X	GAA	AAAGCAAU	AUUGCUUUC GGUAGUGG
	1291	CAUCCCAC	CUGAUGA	X	GAA	ACCGAAAG	CUUUCGGUA GUGGGAUG
	1304	CCACCAAA	CUGAUGA	X	GAA	AUUUCAUC	GAUGAAAUC UUUGGUGG
	1306	UUCCACCA	CUGAUGA	X	GAA	AGAUUUCA	UGAAAUCUU UGGUGGAA
	1307	CUUCCACC	CUGAUGA	X	GAA	AAGAUUUC	GAAAUCUUU GGUGGAAG
25	1330	UCGGACUU	CUGAUGA	X	GAA	ACUGCCCA	UGGGCAGUC AAGUCCGA
	1335	GGGAUUCG	CUGAUGA	X	GAA	ACUUGACU	AGUCAAGUC CGAAUCCC
	1341	UUCACAGG	CUGAUGA	X	GAA	AUUCGGAC	GUCCGAAUC CCUGUGAA
	1352	AACUGAGA	CUGAUGA	X	GAA	ACUUCACA	UGUGAAGUA UCUCAGUU
	1354	GUAACUGA	CUGAUGA	X	GAA	AUACUUCA	UGAAGUAUC UCAGUUAC
30	1356	GGGUAACU	CUGAUGA	X	GAA	AGAUACUU	AAGUAUCUC AGUUACCC

	1360	AGCUGGGU	CUGAUGA	х	GAA	ACUGAGAU	AUCUCAGUU	ACCCAGCU
	1361	GAGCUGGG	CUGAUGA	x	GAA	AACUGAGA	UCUCAGUUA	CCCAGCUC
	1369	GAUAUCAG	CUGAUGA	x	GAA	AGCUGGGU	ACCCAGCUC	CUGAUAUC
	1375	CCAUUUGA	CUGAUGA	x	GAA	AUCAGGAG	CUCCUGAUA	UCAAAUGG
5	1377	UACCAUUU	CUGAUGA	х	GAA	AUAUCAGG	CCUGAUAUC	AAAUGGUA
	1385	CAUUUCUG	CUGAUGA	x	GAA	ACCAUUUG	CAAAUGGUA	CAGAAAUG
	1404	UUGGACUC	CUGAUGA	x	GAA	AUGGGCCU	AGGCCCAUU	GAGUCCAA
	1409	UGUAGUUG	CUGAUGA	х	GAA	ACUCAAUG	CAUUGAGUC	CAACUACA
	1415	UCAUUGUG	CUGAUGA	Х	GAA	AGUUGGAC	GUCCAACUA	CACAAUGA
10	1425	UCGCCAAC	CUGAUGA	X	GAA	AUCAUUGU	ACAAUGAUU	GUUGGCGA
	1428	UCAUCGCC	CUGAUGA	X	GAA	ACAAUCAU	AUGAUUGUU	GGCGAUGA
	1440	AUGAUGGU	CUGAUGA	X	GAA	AGUUCAUC	GAUGAACUC	ACCAUCAU
	1446	ACUUCCAU	CUGAUGA	X	GAA	AUGGUGAG	CUCACCAUC	AUGGAAGU
	1478	UGACCGUG	CUGAUGA	Х	GAA	AGUUUCCU	AGGAAACUA	CACGGUCA
15	1485	GUGAGGAU	CUGAUGA	Х	GAA	ACCGUGUA	UACACGGUC	AUCCUCAC
	1488	UUGGUGAG	CUGAUGA	х	GAA	AUGACCGU	ACGGUCAUC	CUCACCAA
	1491	GGGUUGGU	CUGAUGA	x	GAA	AGGAUGAC	GUCAUCCUC	ACCAACCC
	1503	UCCAUUGA	CUGAUGA	X	GAA	AUGGGGUU	AACCCCAUU	UCAAUGGA
	1504	CUCCAUUG	CUGAUGA	X	GAA	AAUGGGGU	ACCCCAUUU	CAAUGGAG
20	1505	UCUCCAUU	CUGAUGA	X	GAA	AAAUGGGG	CCCCAUUUC	AAUGGAGA
	1530	ACCAGAGA	CUGAUGA	X	GAA	ACCAUGUG	CACAUGGUC	UCUCUGGU
	1532	CAACCAGA	CUGAUGA	X	GAA	AGACCAUG	CAUGGUCUC	UCUGGUUG
	1534	CACAACCA	CUGAUGA	X	GAA	AGAGACCA	UGGUCUCUC	UGGUUGUG
	1539	ACAUUCAC	CUGAUGA	X	GAA	ACCAGAGA	UCUCUGGUU	GUGAAUGU
25	1548	UGGGGUGG	CUGAUGA	X	GAA	ACAUUCAC	GUGAAUGUC	CCACCCCA
	1560	UUCUCACC	CUGAUGA	X	GAA	AUCUGGGG	CCCCAGAUC	GGUGAGAA
	1574	GCGAGAUC	CUGAUGA	X	GAA	AGGCUUUC	GAAAGCCUU	GAUCUCGC
	1578	AUAGGCGA	CUGAUGA	X	GAA	AUCAAGGC	GCCUUGAUC	UCGCCUAU
	1580	CCAUAGGC	CUGAUGA	X	GAA	AGAUCAAG	CUUGAUCUC	GCCUAUGG
30	1585	GGAAUCCA	CUGAUGA	X	GAA	AGGCGAGA	UCUCGCCUA	UGGAUUCC

	1591	CUGGUAGG	CUGAUGA	X	GAA	AUCCAUAG	CUAUGGAUU	CCUACCAG
	1592	ACUGGUAG	CUGAUGA	X	GAA	AAUCCAUA	UAUGGAUUC	CUACCAGU
	1595	CAUACUGG	CUGAUGA	X	GAA	AGGAAUCC	GGAUUCCUA	CCAGUAUG
	1601	UGGUCCCA	CUGAUGA	X	GAA	ACUGGUAG	CUACCAGUA	UGGGACCA
5	1619	UGCAUGUC	CUGAUGA	X	GAA	AUGUCUGC	GCAGACAUU	GACAUGCA
	1632	UUGGCGUA	CUGAUGA	X	GAA	ACUGUGCA	UGCACAGUC	UACGCCAA
	1634	GGUUGGCG	CUGAUGA	X	GAA	AGACUGUG	CACAGUCUA	CGCCAACC
	1645	GUGCAGGG	CUGAUGA	X	GAA	AGGGUUGG	CCAACCCUC	CCCUGCAC
	1659	UACCACUG	CUGAUGA	X	GAA	AUGUGGUG	CACCACAUC	CAGUGGUA
10	1667	GCUGCCAG	CUGAUGA	X	GAA	ACCACUGG	CCAGUGGUA	CUGGCAGC
	1677	GCUUCUUC	CUGAUGA	X	GAA	AGCUGCCA	UGGCAGCUA	GAAGAAGC
	16 91	GUCUGUAG	CUGAUGA	X	GAA	AGCAGGCU	AGCCUGCUC	CUACAGAC
	1694	CGGGUCUG	CUGAUGA	X	GAA	AGGAGCAG	CUGCUCCUA	CAGACCCG
	1718	UACAAGCA	CUGAUGA	X	GAA	ACGGGCUU	AAGCCCGUA	UGCUUGUA
15	17 23	UUCUUUAC	CUGAUGA	X	GAA	AGCAUACG	CGUAUGCUU	GUAAAGAA
	1726	CCAUUCUU	CUGAUGA	X	GAA	ACAAGCAU	AUGCUUGUA	AAGAAUGG
	1750	CCCCUGGA	CUGAUGA	X	GAA	AUCCUCCA	UGGAGGAUU	UCCAGGGG
	1751	CCCCCUGG	CUGAUGA	X	GAA	AAUCCUCC	GGAGGAUUU	CCAGGGGG
	1752	CCCCCCUG	CUGAUGA	X	GAA	AAAUCCUC	GAGGAUUUC	CAGGGGG
20	1770	GUGACUUC	CUGAUGA	X	GAA	AUCUUGUU	AACAAGAUC	GAAGUCAC
	1776	UUUUUGGU	CUGAUGA	X	GAA	ACUUCGAU	AUCGAAGUC	ACCAAAAA
	1790	UCAGGGCA	CUGAUGA	X	GAA	AUUGGUUU	AAACCAAUA	UGCCCUGA
	1800	UUUCCUUC	CUGAUGA	X	GAA	AUCAGGGC	GCCCUGAUU	GAAGGAAA
	1821	AGCGUACU	CUGAUGA	X	GAA	ACAGUUUU	AAAACUGUA	AGUACGCU
25	1825	GACCAGCG	CUGAUGA	X	GAA	ACUUACAG	CUGUAAGUA	CGCUGGUC
	1833	GCUUGGAU	CUGAUGA	X	GAA	ACCAGCGU	ACGCUGGUC	AUCCAAGC
	1836	GCAGCUUG	CUGAUGA	X	GAA	AUGACCAG	CUGGUCAUC	CAAGCUGC
	1853	ACAACGCU	CUGAUGA	X	GAA	ACACGUUG	CAACGUGUC .	AGCGUUGU
	1859	AUUUGUAC	CUGAUGA	X	GAA	ACGCUGAC	GUCAGCGUU	GUACAAAU
30	1862	CACAUUUG	CUGAUGA	X	GAA	ACAACGCU	AGCGUUGUA	CAAAUGUG

PCT/US96/17480

WO 97/15662

	1878	GCUUUGUU	CUGAUGA	X	GAA	AUGGCUUC	GAAGCCAUC	AACAAAGC
	1905	AAGGAGAU	CUGAUGA	X	GAA	ACCCUCUC	GAGAGGGUC	AUCUCCUU
	1908	UGGAAGGA	CUGAUGA	X	GAA	AUGACCCU	AGGGUCAUC	UCCUUCCA
	1910	CAUGGAAG	CUGAUGA	X	GAA	AGAUGACC	GGUCAUCUC	CUUCCAUG
5	1913	UCACAUGG	CUGAUGA	X	GAA	AGGAGAUG	CAUCUCCUU	CCAUGUGA
	1914	AUCACAUG	CUGAUGA	x	GAA	AAGGAGAU	AUCUCCUUC	CAUGUGAU
	1923	GGACCCCU	CUGAUGA	X	GAA	AUCACAUG	CAUGUGAUC	AGGGGUCC
	1930	AAUUUCAG	CUGAUGA	X	GAA	ACCCCUGA	UCAGGGGUC	CUGAAAUU
	1938	UGCACAGU	CUGAUGA	x	GAA	AUUUCAGG	CCUGAAAUU	ACUGUGCA
10	1939	UUGCACAG	CUGAUGA	X	GAA	AAUUUCAG	CUGAAAUUA	CUGUGCAA
	1982	ACAACAGG	CUGAUGA	X	GAA	ACACACUC	GAGUGUGUC	CCUGUUGU
	1988	CAGUGCAC	CUGAUGA	X	GAA	ACAGGGAC	GUCCCUGUU	GUGCACUG
	2008	CUCAAACG	CUGAUGA	X	GAA	AUUUCUGU	ACAGAAAUA	CGUUUGAG
	2012	GGUUCUCA	CUGAUGA	X	GAA	ACGUAUUU	AAAUACGUU	UGAGAACC
15	2013	AGGUUCUC	CUGAUGA	X	GAA	AACGUAUU	AAUACGUUU	GAGAACCU
	2022	UACCACGU	CUGAUGA	X	GAA	AGGUUCUC	GAGAACCUC	ACGUGGUA
	2030	CAAGCUUG	CUGAUGA	X	GAA	ACCACGUG	CACGUGGUA	CAAGCUUG
	2037	UGUGAGCC	CUGAUGA	X	GAA	AGCUUGUA	UACAAGCUU	GGCUCACA
	2042	UUGCCUGU	CUGAUGA	X	GAA	AGCCAAGC	GCUUGGCUC	ACAGGCAA
20	2054	UGUGGACC	CUGAUGA	X	GAA	AUGUUGCC	GGCAACAUC	GGUCCACA
	2058	CCCAUGUG	CUGAUGA	X	GAA	ACCGAUGU	ACAUCGGUC	CACAUGGG
	2072	GUGUGAGU	CUGAUGA	X	GAA	AUUCGCCC	GGGCGAAUC	ACUCACAC
	2076	ACUGGUGU	CUGAUGA	X	GAA	AGUGAUUC	GAAUCACUC	ACACCAGU
	2085	UUCUUGCA	CUGAUGA	X	GAA	ACUGGUGU	ACACCAGUU	UGCAAGAA
2 5	2086	GUUCUUGC	CUGAUGA	X	GAA	AACUGGUG	CACCAGUUU	GCAAGAAC
	2096	GAGCAUCC	CUGAUGA	X	GAA	AGUUCUUG	CAAGAACUU	GGAUGCUC
	2104	UUUCCAAA	CUGAUGA	X	GAA	AGCAUCCA	UGGAUGCUC	UUUGGAAA
	2106	AGUUUCCA	CUGAUGA	X	GAA	AGAGCAUC	GAUGCUCUU	UGGAAACU
	2107	CAGUUUCC	CUGAUGA	X	GAA	AAGAGCAU	AUGCUCUUU	GGAAACUG
30	2129	UGUUAGAA	CUGAUGA	X	GAA	ACAUGGUG	CACCAUGUU	UUCUAACA

	2130	CUGUUAGA	CUGAUGA	X	GAA	AACAUGGU	ACCAUGUUU	UCUAACAG
	2131	GCUGUUAG	CUGAUGA	X	GAA	AAACAUGG	CCAUGUUUU	CUAACAGC
	2132	UGCUGUUA	CUGAUGA	X	GAA	AAAACAUG	CAUGUUUUC	UAACAGCA
	2134	UGUGCU GU	CUGAUGA	X	GAA	AGAAAACA	UGUUUUCUA	ACAGCACA
5	2151	ACAAUCAA	CUGAUGA	X	GAA	AUGUCAUU	AAUGACAUC	UUGAUUGU
	2153	CCACAAUC	CUGAUGA	X	GAA	AGAUGUCA	UGACAUCUU	GAUUGUGG
	2157	AAUGCCAC	CUGAUGA	X	GAA	AUCAAGAU	AUCUUGAUU	GUGGCAUU
	2165	CAUUCUGA	CUGAUGA	X	GAA	AUGCCACA	UGUGGCAUU	UCAGAAUG
	2166	GCAUUCUG	CUGAUGA	Х	GAA	AAUGCCAC	GUGGCAUUU	CAGAAUGC
10	2167	GGCAUUCU	CUGAUGA	Х	GAA	AAAUGCCA	UGGCAUUUC	AGAAUGCC
	2177	CCUGCAGA	CUGAUGA	X	GAA	AGGCAUUC	GAAUGCCUC	UCUGCAGG
	2179	GUCCUGCA	CUGAUGA	X	GAA	AGAGGCAU	AUGCCUCUC	UGCAGGAC
	2198	AGCAAACA	CUGAUGA	X	GAA	AGUCGCCU	AGGCGACUA	UGUUUGCU
	2202	GCAGAGCA	CUGAUGA	X	GAA	ACAUAGUC	GACUAUGUU	UGCUCUGC
15	2203	AGCAGAGC	CUGAUGA	X	GAA	AACAUAGU	ACUAUGUUU	GCUCUGCU
	2207	CUUGAGCA	CUGAUGA	X	GAA	AGCAAACA	UGUUUGCUC	UGCUCAAG
	2212	CUUAUCUU	CUGAUGA	X	GAA	AGCAGAGC	GCUCUGCUC	AAGAUAAG
	2218	GGUCUUCU	CUGAUGA	X	GAA	AUCUUGAG	CUCAAGAUA	AGAAGACC
	2239	GACCAGGC	CUGAUGA	X	GAA	AUGUCUUU	AAAGACAUU	GCCUGGUC
20	2247	AGCUGUUU	CUGAUGA	X	GAA	ACCAGGCA	UGCCUGGUC	AAACAGCU
	2256	AGGAUGAU	CUGAUGA	X	GAA	AGCUGUUU	AAACAGCUC	AUCAUCCU
	2259	UCUAGGAU	CUGAUGA	X	GAA	AUGAGCUG	CAGCUCAUC	AUCCUAGA
	2262	CGCUCUAG	CUGAUGA	X	GAA	AUGAUGAG	CUCAUCAUC	CUAGAGCG
	2265	AUGCGCUC	CUGAUGA	X	GAA	AGGAUGAU	AUCAUCCUA	GAGCGCAU
25	2286	UUUCCGGU	CUGAUGA	X	GAA	AUCAUGGG	CCCAUGAUC	ACCGGAAA
	2296	AUUCUCCA	CUGAUGA	X	GAA	AUUUCCGG	CCGGAAAUC	UGGAGAAU
	2305	UGUUGUCU	CUGAUGA	X	GAA	AUUCUCCA	UGGAGAAUC	AGACAACA
	2319	GUCUCGCC	CUGAUGA	X	GAA	AUGGUUGU	ACAACCAUU	GGCGAGAC
	2331	GUCACUUC	CUGAUGA	X	GAA	AUGGUCUC	GAGACCAUU	GAAGUGAC
30	2341	UGCUGGGC	CUGAUGA	X	GAA	AGUCACUU	AAGUGACUU	GCCCAGCA

	2351	GAUUUCCA	CUGAUGA	X	GAA	AUGCUGGG	CCCAGCAUC	UGGAAAUC
	2359	UGGGGUAG	CUGAUGA	X	GAA	AUUUCCAG	CUGGAAAUC	CUACCCCA
	2362	GUGUGGGG	CUGAUGA	X	GAA	AGGAUUUC	GAAAUCCUA	CCCCACAC
	2373	AACCAUGU	CUGAUGA	X	GAA	AUGUGUGG	CCACACAUU	ACAUGGUU
5	2374	GAACCAUG	CUGAUGA	X	GAA	AAUGUGUG	CACACAUUA	CAUGGUUC
	2381	UGUCUUUG	CUGAUGA	X	GAA	ACCAUGUA	UACAUGGUU	CAAAGACA
	2382	UUGUCUUU	CUGAUGA	X	GAA	AACCAUGU	ACAUGGUUC	AAAGACAA
	2403	GAAUCUUC	CUGAUGA	X	GAA	ACCAGGGU	ACCCUGGUA	GAAGAUUC
	2410	AAUGCCUG	CUGAUGA	X	GAA	AUCUUCUA	UAGAAGAUU	CAGGCAUU
10	2411	CAAUGCCU	CUGAUGA	X	GAA	AAUCUUCU	AGAAGAUUC	AGGCAUUG
	2418	CUCAGUAC	CUGAUGA	X	GAA	AUGCCUGA	UCAGGCAUU	GUACUGAG
	2421	UCUCUCAG	CUGAUGA	X	GAA	ACAAUGCC	GGCAUUGUA	CUGAGAGA
	2449	CCUGCGGA	CUGAUGA	X	GAA	AGUCAGGU	ACCUGACUA	UCCGCAGG
	2451	ACCCUGCG	CUGAUGA	X	GAA	AUAGUCAG	CUGACUAUC	CGCAGGGU
15	2481	CAGGUGUA	CUGAUGA	X	GAA	AGGCCUCC	GGAGGCCUC	UACACCUG
	2483	GGCAGGUG	CUGAUGA	X	GAA	AGAGGCCU	AGGCCUCUA	CACCUGCC
	2505	CAGCCAAG	CUGAUGA	X	GAA	ACAUUGCA	UGCAAUGUC	CUUGGCUG
	2508	GCACAGCC	CUGAUGA	X	GAA	AGGACAUU	AAUGUCCUU	GGCUGUGC
	2532	AUUAUGAA	CUGAUGA	X	GAA	AGCGUCUC	GAGACGCUC	UUCAUAAU
20	2534	CUAUUAUG	CUGAUGA	X	GAA	AGAGCGUC	GACGCUCUU	CAUAAUAG
	2535	UCUAUUAU	CUGAUGA	X	GAA	AAGAGCGU	ACGCUCUUC	AUAAUAGA
	2538	CCUUCUAU	CUGAUGA	X	GAA	AUGAAGAG	CUCUUCAUA	AUAGAAGG
	2541	GCACCUUC	CUGAUGA	X	GAA	AUUAUGAA	UUCAUAAUA	GAAGGUGC
	2567	UGACUUCC	CUGAUGA	X	GAA	AGUUGGUC	GACCAACUU	GGAAGUCA
25	2574	AGGAUAAU	CUGAUGA	X	GAA	ACUUCCAA	UUGGAAGUC	AUUAUCCU
	2577	ACGAGGAU	CUGAUGA	X	GAA	AUGACUUC	GAAGUCAUU	AUCCUCGU
	2578	GACGAGGA	CUGAUGA	X	GAA	AAUGACUU	AAGUCAUUA	UCCUCGUC
	2580	CCGACGAG	CUGAUGA	X	GAA	AUAAUGAC	GUCAUUAUC	CUCGUCGG
	2583	GUGCCGAC	CUGAUGA	X	GAA	AGGAUAAU	AUUAUCCUC	GUCGGCAC
30	2586	GCAGUGCC	CUGAUGA	X	GAA	ACGAGGAU	AUCCUCGUC	GGCACUGC

	2601	AACAUGGC	CUGAUGA	Х	GAA	AUCACUGC	GCAGUGAUU	GCCAUGUU
	2609	GCCAGAAG	CUGAUGA	X	GAA	ACAUGGCA	UGCCAUGUU	CUUCUGGC
	2610	AGCCAGAA	CUGAUGA	X	GAA	AACAUGGC	GCCAUGUUC	UUCUGGCU
	2612	GGAGCCAG	CUGAUGA	X	GAA	AGAACAUG	CAUGUUCUU	CUGGCUCC
5	2613	AGGAGCCA	CUGAUGA	X	GAA	AAGAACAU	AUGUUCUUC	UGGCUCCU
	2619	ACAAGAAG	CUGAUGA	X	GAA	AGCCAGAA	UUCUGGCUC	CUUCUUGU
	2622	AUGACAAG	CUGAUGA	X	GAA	AGGAGCCA	UGGCUCCUU	CUUGUCAU
	2623	AAUGACAA	CUGAUGA	X	GAA	AAGGAGCC	GGCUCCUUC	UUGUCAUU
	2625	ACAAUGAC	CUGAUGA	X	GAA	AGAAGGAG	CUCCUUCUU	GUCAUUGU
10	2628	AGGACAAU	CUGAUGA	X	GAA	ACAAGAAG	CUUCUUGUC	AUUGUCCU
	2631	CGUAGGAC	CUGAUGA	X	GAA	AUGACAAG	CUUGUCAUU	GUCCUACG
	2634	GUCCGUAG	CUGAUGA	X	GAA	ACAAUGAC	GUCAUUGUC	CUACGGAC
	2637	ACGGUCCG	CUGAUGA	X	GAA	AGGACAAU	AUUGUCCUA	CGGACCGU
	2646	GCCCGCUU	CUGAUGA	X	GAA	ACGGUCCG	CGGACCGUU	AAGCGGGC
15	2647	GGCCCGCU	CUGAUGA	X	GAA	AACGGUCC	GGACCGUUA	AGCGGGCC
	2681	UAGACAAG	CUGAUGA	X	GAA	AGCCUGUC	GACAGGCUA	CUUGUCUA
	2684	CAAUAGAC	CUGAUGA	X	GAA	AGUAGCCU	AGGCUACUU	GUCUAUUG
	2687	UGACAAUA	CUGAUGA	X	GAA	ACAAGUAG	CUACUUGUC	UAUUGUCA
	2689	CAUGACAA	CUGAUGA	X	GAA	AGACAAGU	ACUUGUCUA	UUGUCAUG
20	2691	UCCAUGAC	CUGAUGA	X	GAA	AUAGACAA	UUGUCUAUU	GUCAUGGA
	2694	GGAUCCAU	CUGAUGA	X	GAA	ACAAUAGA	UCUAUUGUC	AUGGAUCC
	2701	UUCAUCUG	CUGAUGA	X	GAA	AUCCAUGA	UCAUGGAUC	CAGAUGAA
	2711	CCAAGGGC	CUGAUGA	X	GAA	AUUCAUCU	AGAUGAAUU	GCCCUUGG
	2717	GCUCAUCC	CUGAUGA	X	GAA	AGGGCAAU	AUUGCCCUU	GGAUGAGC
25	2738	CAUAAGGC	CUGAUGA	X	GAA	AGCGUUCA	UGAACGCUU	GCCUUAUG
	2743	GGCAUCAU	CUGAUGA	X	GAA	AGGCAAGC	GCUUGCCUU	AUGAUGCC
	2744	UGGCAUCA	CUGAUGA	X	GAA	AAGGCAAG	CUUGCCUUA	UGAUGCCA
	2765	CCCUGGGG	CUGAUGA	X	GAA	AUUCCCAC	GUGGGAAUU	CCCCAGGG
	2766	UCCCUGGG	CUGAUGA	X	GAA	AAUUCCCA	UGGGAAUUC	CCCAGGGA
30	2787	GGUUUUCC	CUGAUGA	X	GAA	AGUUUCAG	CUGAAACUA	GGAAAACC

	2797	GCGGCCAA	CUGAUGA	X	GAA	AGGUUUUC	GAAAACCUC	UUGGCCGC
	2799	CCGCGGCC	CUGAUGA	X	GAA	AGAGGUUU	AAACCUCUU	GGCCGCGG
	2813	CUUGGCCG	CUGAUGA	X	GAA	AGGCACCG	CGGUGCCUU	CGGCCAAG
	2814	ACUUGGCC	CUGAUGA	X	GAA	AAGGCACC	GGUGCCUUC	GGCCAAGU
5	2826	UCUGCCUC	CUGAUGA	X	GAA	AUCACUUG	CAAGUGAUU	GAGGCAGA
	2839	AAUUCCAA	CUGAUGA	X	GAA	AGCGUCUG	CAGACGCUU	UUGGAAUU
	2840	CAAUUCCA	CUGAUGA	X	GAA	AAGCGUCU	AGACGCUUU	UGGAAUUG
	2841	UCAAUUCC	CUGAUGA	X	GAA	AAAGCGUC	GACGCUUUU	GGAAUUGA
	2847	GUCUUGUC	CUGAUGA	X	GAA	AUUCCAAA	UUUGGAAUU	GACAAGAC
10	2863	UGUUUUGC	CUGAUGA	X	GAA	AGUCGCUG	CAGCGACUU	GCAAAACA
	2874	UUGACGGC	CUGAUGA	X	GAA	ACUGUUUU	AAAACAGUA	GCCGUCAA
	2880	AACAUCUU	CUGAUGA	X	GAA	ACGGCUAC	GUAGCCGUC	AAGAUGUU
	2888	cuucuuuc	CUGAUGA	X	GAA	ACAUCUUG	CAAGAUGUU	GAAAGAAG
	2917	GAGGGCUC	CUGAUGA	X	GAA	AUGCUCGC	GCGAGCAUC	GAGCCCUC
15	2925	UCAGACAU	CUGAUGA	X	GAA	AGGGCUCG	CGAGCCCUC	AUGUCUGA
	2930	UGAGUUCA	CUGAUGA	X	GAA	ACAUGAGG	CCUCAUGUC	UGAACUCA
	2937	AGGAUCUU	CUGAUGA	X	GAA	AGUUCAGA	UCUGAACUC	AAGAUCCU
	2943	UGGAUGAG	CUGAUGA	X	GAA	AUCUUGAG	CUCAAGAUC	CUCAUCCA
	2946	AUGUGGAU	CUGAUGA	X	GAA	AGGAUCUU	AAGAUCCUC	AUCCACAU
20	2949	CCAAUGUG	CUGAUGA	X	GAA	AUGAGGAU	AUCCUCAUC	CACAUUGG
	2955	UGGUGACC	CUGAUGA	X	GAA	AUGUGGAU	AUCCACAUU	GGUCACCA
	2959	GAGAUGGU	CUGAUGA	X	GAA	ACCAAUGU	ACAUUGGUC	ACCAUCUC
	2965	CACAUUGA	CUGAUGA	X	GAA	AUGGUGAC	GUCACCAUC	UCAAUGUG
	2967	ACCACAUU	CUGAUGA	X	GAA	AGAUGGUG	CACCAUCUC	AAUGUGGU
25	2982	GCGCCUAG	CUGAUGA	X	GAA	AGGUUCAC	GUGAACCUC	CUAGGCGC
	2985	CAGGCGCC	CUGAUGA	X	GAA	AGGAGGUU	AACCUCCUA	GGCGCCUG
	3013	CACCAUGA	CUGAUGA	X	GAA	AGGCCCUC	GAGGGCCUC	UCAUGGUG
	3015	AUCACCAU	CUGAUGA	X	GAA	AGAGGCCC	GGGCCUCUC	AUGGUGAU
	3024	AAUUCCAC	CUGAUGA	X	GAA	AUCACCAU	AUGGUGAUU	GUGGAAUU
30	3032	ACUUGCAG	CUGAUGA	X	GAA	AUUCCACA	UGUGGAAUU	CUGCAAGU

	3033	AACUUGCA	CUGAUGA	. х	GAA	AAUUCCAC	GUGGAAUUC UGCAAGUU
	3041	GGUUUCCA	CUGAUGA	. X	GAA	ACUUGCAG	CUGCAAGUU UGGAAACC
	3042	AGGUUUCC	CUGAUGA	X	GAA	AACUUGCA	UGCAAGUUU GGAAACCU
	3051	UAAGUUGA	CUGAUGA	X	GAA	AGGUUUCC	GGAAACCUA UCAACUUA
5	3053	AGUAAGUU	CUGAUGA	X	GAA	AUAGGUUU	AAACCUAUC AACUUACU
	3058	CCGUAAGU	CUGAUGA	X	GAA	AGUUGAUA	UAUCAACUU ACUUACGG
	3059	CCCGUAAG	CUGAUGA	X	GAA	AAGUUGAU	AUCAACUUA CUUACGGG
	3062	UGCCCCGU	CUGAUGA	X	GAA	AGUAAGUU	AACUUACUU ACGGGGCA
	3063	UUGCCCCG	CUGAUGA	X	GAA	AAGUAAGU	ACUUACUUA CGGGGCAA
10	3083	AGGGAACA	CUGAUGA	X	GAA	AUUCAUUU	AAAUGAAUU UGUUCCCU
	3084	UAGGGAAC	CUGAUGA	X	GAA	AAUUCAUU	AAUGAAUUU GUUCCCUA
	3087	UUAUAGGG	CUGAUGA	Х	GAA	ACAAAUUC	GAAUUUGUU CCCUAUAA
	3088	CUUAUAGG	CUGAUGA	X	GAA	AACAAAUU	AAUUUGUUC CCUAUAAG
	3092	UGCUCUUA	CUGAUGA	X	GAA	AGGGAACA	UGUUCCCUA UAAGAGCA
15	3094	UUUGCUCU	CUGAUGA	X	GAA	AUAGGGAA	UUCCCUAUA AGAGCAAA
	3113	CCUGGCGG	CUGAUGA	X	GAA	AGCGUGCC	GGCACGCUU CCGCCAGG
	3114	CCCUGGCG	CUGAUGA	X	GAA	AAGCGUGC	GCACGCUUC CGCCAGGG
	3131	CCCCAACG	CUGAUGA	X	GAA	AGUCCUUG	CAAGGACUA CGUUGGGG
	3135	AGCUCCCC	CUGAUGA	X	GAA	ACGUAGUC	GACUACGUU GGGGAGCU
20	3144	UCCACGGA	CUGAUGA	X	GAA	AGCUCCCC	GGGGAGCUC UCCGUGGA
	3146	GAUCCACG	CUGAUGA	X	GAA	AGAGCUCC	GGAGCUCUC CGUGGAUC
	3154	UCUUUUCA	CUGAUGA	X	GAA	AUCCACGG	CCGUGGAUC UGAAAAGA
	3167	UGCUGUCC	CUGAUGA	X	GAA	AGCGUCUU	AAGACGCUU GGACAGCA
	3177	CUGCUGGU	CUGAUGA	X	GAA	AUGCUGUC	GACAGCAUC ACCAGCAG
25	3194	AGCUGGCA	CUGAUGA	X	GAA	AGCUCUGG	CCAGAGCUC UGCCAGCU
	3203	CAAAGCCU	CUGAUGA	X	GAA	AGCUGGCA	UGCCAGCUC AGGCUUUG
	3209	CCUCAACA	CUGAUGA	X	GAA	AGCCUGAG	CUCAGGCUU UGUUGAGG
							UCAGGCUUU GUUGAGGA
							GGCUUUGUU GAGGAGAA
30	3224	CACUGAGC	CUGAUGA	X	GAA	AUUUCUCC	GGAGAAAUC GCUCAGUG

	3228	ACAUCACU	CUGAUGA	X	GAA	AGCGAUUU	AAAUCGCUC	AGUGAUGU
	3237	UCUUCCUC	CUGAUGA	X	GAA	ACAUCACU	AGUGAUGUA	GAGGAAGA
	3253	UUCUUCAG	CUGAUGA	X	GAA	AGCUUCUU	AAGAAGCUU	CUGAAGAA
	3254	GUUCUUCA	CUGAUGA	X	GAA	AAGCUUCU	AGAAGCUUC	UGAAGAAC
5	3266	AGUCCUUG	CUGAUGA	X	GAA	ACAGUUCU	AGAACUGUA	CAAGGACU
	3275	AGGUCAGG	CUGAUGA	X	GAA	AGUCCUUG	CAAGGACUU	CCUGACCU
	3276	AAGGUCAG	CUGAUGA	X	GAA	AAGUCCUU	AAGGACUUC	CUGACCUU
	3284	GAUGCUCC	CUGAUGA	X	GAA	AGGUCAGG	CCUGACCUU	GGAGCAUC
	3292	ACAGAUGA	CUGAUGA	X	GAA	AUGCUCCA	UGGAGCAUC	UCAUCUGU
10	3294	UAACAGAU	CUGAUGA	X	GAA	AGAUGCUC	GAGCAUCUC	AUCUGUUA
	3297	CUGUAACA	CUGAUGA	X	GAA	AUGAGAUG	CAUCUCAUC	UGUUACAG
	3301	GAAGCUGU	CUGAUGA	X	GAA	ACAGAUGA	UCAUCUGUU	ACAGCUUC
	3302	GGAAGCUG	CUGAUGA	X	GAA	AACAGAUG	CAUCUGUUA	CAGCUUCC
	3308	CCACUUGG	CUGAUGA	X	GAA	AGCUGUAA	UUACAGCUU	CCAAGUGG
15	3309	GCCACUUG	CUGAUGA	X	GAA	AAGCUGUA	UACAGCUUC	CAAGUGGC
	3319	CAUGCCCU	CUGAUGA	X	GAA	AGCCACUU	AAGUGGCUA	AGGGCAUG
	3332	AUGCCAAG	CUGAUGA	X	GAA	ACUCCAUG	CAUGGAGUU	CUUGGCAU
	3333	GAUGCCAA	CUGAUGA	X	GAA	AACUCCAU	AUGGAGUUC	UUGGCAUC
	3335	UUGAUGCC	CUGAUGA	X	GAA	AGAACUCC	GGAGUUCUU	GGCAUCAA
20	3341	ACUUCCUU	CUGAUGA	X	GAA	AUGCCAAG	CUUGGCAUC	AAGGAAGU
	3352	CCUGUGGA	CUGAUGA	X	GAA	ACACUUCC	GGAAGUGUA	UCCACAGG
	3354	UCCCUGUG	CUGAUGA	X	GAA	AUACACUU	AAGUGUAUC	CACAGGGA
	3381	GAUAGGAG	CUGAUGA	X	GAA	AUGUUUCG	CGAAACAUU	CUCCUAUC
	3382	CGAUAGGA	CUGAUGA	X	GAA	AAUGUUUC	GAAACAUUC	UCCUAUCG
25	3384	UCCGAUAG	CUGAUGA	X	GAA	AGAAUGUU	AACAUUCUC	CUAUCGGA
	3387	UUCUCCGA	CUGAUGA	X	GAA	AGGAGAAU	AUUCUCCUA	UCGGAGAA
	3389	UCUUCUCC	CUGAUGA	X	GAA	AUAGGAGA	UCUCCUAUC	GGAGAAGA
	3405	CAGAUCUU	CUGAUGA	X	GAA	ACCACAUU	AAUGUGGUU	AAGAUCUG
	3406	ACAGAUCU	CUGAUGA	X	GAA	AACCACAU	AUGUGGUUA	AGAUCUGU
30	3411	AAGUCACA	CUGAUGA	X	GAA	AUCUUAAC	GUUAAGAUC	UGUGACUU

	3419	CCAAGCCG	CUGAUGA	X	GAA	AGUCACAG	CUGUGACUU	CGGCUUGG
	3420	GCCAAGCC	CUGAUGA	X	GAA	AAGUCACA	UGUGACUUC	GGCUUGGC
	3425	CCCGGGCC	CUGAUGA	X	GAA	AGCCGAAG	CUUCGGCUU	GGCCCGGG
	3438	UCUUUAUA	CUGAUGA	X	GAA	AUGUCCCG	CGGGACAUU	UAUAAAGA
5	3439	GUCUUUAU	CUGAUGA	X	GAA	AAUGUCCC	GGGACAUUU	AUAAAGAC
	3440	GGUCUUUA	CUGAUGA	X	GAA	AAAUGUCC	GGACAUUUA	UAAAGACC
	3442	CGGGUCUU	CUGAUGA	X	GAA	AUAAAUGU	ACAUUUAUA	AAGACCCG
	3 4 54	UCUGACAU	CUGAUGA	X	GAA	AUCCGGGU	ACCCGGAUU	AUGUCAGA
	3455	UUCUGACA	CUGAUGA	X	GAA	AAUCCGGG	CCCGGAUUA	UGUCAGAA
10	3459	CCUUUUCU	CUGAUGA	X	GAA	ACAUAAUC	GAUUAUGUC	AGAAAAGG
	3480	UUCAAAGG	CUGAUGA	X	GAA	AGUCGGGC	GCCCGACUC	CCUUUGAA
	3484	CCACUUCA	CUGAUGA	X	GAA	AGGGAGUC	GACUCCCUU	UGAAGUGG
	3485	UCCACUUC	CUGAUGA	X	GAA	AAGGGAGU	ACUCCCUUU	GAAGUGGA
	3510	CUGUCAAA	CUGAUGA	X	GAA	AUGGUUUC	GAAACCAUU	UUUGACAG
15	3511	UCUGUCAA	CUGAUGA	X	GAA	AAUGGUUU	AAACCAUUU	UUGACAGA
	3512	CUCUGUCA	CUGAUGA	X	GAA	AAAUGGUU	AACCAUUUU	UGACAGAG
	3513	ACUCUGUC	CUGAUGA	X	GAA	AAAAUGGU	ACCAUUUUU	GACAGAGU
	3522	AUUGUGUA	CUGAUGA	X	GAA	ACUCUGUC	GACAGAGUA	UACACAAU
	3524	GAAUUGUG	CUGAUGA	X	GAA	AUACUCUG	CAGAGUAUA	CACAAUUC
20	3531	UCGCUCUG	CUGAUGA	X	GAA	AUUGUGUA	UACACAAUU	CAGAGCGA
	3532	AUCGCUCU	CUGAUGA	X	GAA	AAUUGUGU	ACACAAUUC	AGAGCGAU
	3548	CACCGAAA	CUGAUGA	X	GAA	ACCACACA	UGUGUGGUC	UUUCGGUG
	3550	CACACCGA	CUGAUGA	X	GAA	AGACCACA	UGUGGUCUU	UCGGUGUG
	3551	ACACACCG	CUGAUGA	X	GAA	AAGACCAC	GUGGUCUUU	CGGUGUGU
25	3552	AACACACC	CUGAUGA	X	GAA	AAAGACCA	UGGUCUUUC	GGUGUGUU
	3560	CCCAGAGC	CUGAUGA	X	GAA	ACACACCG	CGGUGUGUU	GCUCUGGG
	3564	AUUUCCCA	CUGAUGA	X	GAA	AGCAACAC	GUGUUGCUC	UGGGAAAU
	3573	AAGGAAAA	CUGAUGA	X	GAA	AUUUCCCA	UGGGAAAUA	UUUUCCUU
	3575	CUAAGGAA	CUGAUGA	X	GAA	AUAUUUCC	GGAAAUAUU	UUCCUUAG
30	3576	CCUAAGGA	CUGAUGA	X	GAA	AAUAUUUC	GAAAUAUUU	UCCUUAGG

	3577	ACCUAAGG	CUGAUGA	X	GAA	AAAUAUUU	AAAUAUUUU	CCUUAGGU
	3578	CACCUAAG	CUGAUGA	X	GAA	UUAUAAAA	AAUAUUUUC	CUUAGGUG
	3581	AGGCACCU	CUGAUGA	X	GAA	AGGAAAAU	AUUUUCCUU	AGGUGCCU
	3582	GAGGCACC	CUGAUGA	X	GAA	AAGGAAAA	UUUUCCUUA	GGUGCCUC
5	3590	GGUAUGGG	CUGAUGA	x	GAA	AGGCACCU	AGGUGCCUC	CCCAUACC
	3596	CCCCAGGG	CUGAUGA	X	GAA	AUGGGGAG	CUCCCCAUA	CCCUGGGG
	3606	UCAAUCUU	CUGAUGA	x	GAA	ACCCCAGG	CCUGGGGUC	AAGAUUGA
	3612	UCUUCAUC	CUGAUGA	x	GAA	AUCUUGAC	GUCAAGAUU	GAUGAAGA
	3623	UCCUACAA	CUGAUGA	X	GAA	AUUCUUCA	UGAAGAAUU	UUGUAGGA
10	3624	CUCCUACA	CUGAUGA	X	GAA	AAUUCUUC	GAAGAAUUU	UGUAGGAG
	3625	UCUCCUAC	CUGAUGA	X	GAA	AAAUUCUU	AAGAAUUUU	GUAGGAGA
	3628	CAAUCUCC	CUGAUGA	X	GAA	ACAAAAUU	AAUUUUGUA	GGAGAUUG
	363 5	CUUCUUUC	CUGAUGA	x	GAA	AUCUCCUA	UAGGAGAUU	GAAAGAAG
	3649	CCGCAUUC	CUGAUGA	X	GAA	AGUUCCUU	AAGGAACUA	GAAUGCGG
15	3661	GUAGUCAG	CUGAUGA	x	GAA	AGCCCGCA	UGCGGGCUC	CUGACUAC
	3668	GGGUAGUG	CUGAUGA	X	GAA	AGUCAGGA	UCCUGACUA	CACUACCC
	3673	UUCUGGGG	CUGAUGA	X	GAA	AGUGUAGU	ACUACACUA	CCCCAGAA
	3686	UGGUCUGG	CUGAUGA	X	GAA	ACAUUUCU	AGAAAUGUA	CCAGACCA
	3734	CUGAAAAC	CUGAUGA	X	GAA	AGGGUCUC	GAGACCCUC	GUUUUCAG
20	3737	ACUCUGAA	CUGAUGA	X	GAA	ACGAGGGU	ACCCUCGUU	UUCAGAGU
	3738	AACUCUGA	CUGAUGA	X	GAA	AACGAGGG	CCCUCGUUU	UCAGAGUU
	3739	CAACUCUG	CUGAUGA	X	GAA	AAACGAGG	CCUCGUUUU	CAGAGUUG
	3740	CCAACUCU	CUGAUGA	X	GAA	AAAACGAG	CUCGUUUUC	AGAGUUGG
	3746	GCUCCACC	CUGAUGA	X	GAA	ACUCUGAA	UUCAGAGUU	GGUGGAGC
25	3757	GUUUCCCA	CUGAUGA	X	GAA	AUGCUCCA	UGGAGCAUU	UGGGAAAC
	3758	GGUUUCCC	CUGAUGA	x	GAA	AAUGCUCC	GGAGCAUUU	GGGAAACC
	3768	GCUUGCAG	CUGAUGA	X	GAA	AGGUUUCC	GGAAACCUC	CUGCAAGC
	3803	GAACAAUA	CUGAUGA	X	GAA	AGUCUUUG	CAAAGACUA	UAUUGUUC
	3805	AAGAACAA	CUGAUGA	X	GAA	AUAGUCUU	AAGACUAUA	UUGUUCUU
30	3807	GGAAGAAC	CUGAUGA	X	GAA	AUAUAGUC	GACUAUAUU	GUUCUUCC

	3810	AUUGGAAG	CUGAUGA	X	GAA	ACAAUAUA	UAUAUUGUU	CUUCCAAU
	3811	CAUUGGAA	CUGAUGA	X	GAA	AACAAUAU	AUAUUGUUC	UUCCAAUG
	3813	GACAUUGG	CUGAUGA	X	GAA	AGAACAAU	AUUGUUCUU	CCAAUGUC
	3814	UGACAUUG	CUGAUGA	X	GAA	AAGAACAA	UUGUUCUUC	CAAUGUCA
5	3821	GUGUCUCU	CUGAUGA	X	GAA	ACAUUGGA	UCCAAUGUC	AGAGACAC
	3847	GAGUCCAG	CUGAUGA	X	GAA	AUCCUCUU	AAGAGGAUU	CUGGACUC
	3848	AGAGUCCA	CUGAUGA	X	GAA	AAUCCUCU	AGAGGAUUC	UGGACUCU
	3855	GGCAGGGA	CUGAUGA	X	GAA	AGUCCAGA	UCUGGACUC	UCCCUGCC
	3857	UAGGCAGG	CUGAUGA	X	GAA	AGAGUCCA	UGGACUCUC	CCUGCCUA
10	3865	AGGUGAGG	CUGAUGA	X	GAA	AGGCAGGG	CCCUGCCUA	CCUCACCU
	3869	AAACAGGU	CUGAUGA	X	GAA	AGGUAGGC	GCCUACCUC	ACCUGUUU
	3876	AUACAGGA	CUGAUGA	X	GAA	ACAGGUGA	UCACCUGUU	UCCUGUAU
	3877	CAUACAGG	CUGAUGA	X	GAA	AACAGGUG	CACCUGUUU	CCUGUAUG
	3878	CCAUACAG	CUGAUGA	X	GAA	AAACAGGU	ACCUGUUUC	CUGUAUGG
15	3883	UUCCUCCA	CUGAUGA	X	GAA	ACAGGAAA	UUUCCUGUA	UGGAGGAA
	3914	CAUAAUGG	CUGAUGA	X	GAA	AUUUGGGG	CCCCAAAUU	CCAUUAUG
	3915	UCAUAAUG	CUGAUGA	X	GAA	AAUUUGGG	CCCAAAUUC	CAUUAUGA
	3919	GUUGUCAU	CUGAUGA	X	GAA	AUGGAAUU	AAUUCCAUU	AUGACAAC
	3920	UGUUGUCA	CUGAUGA	X	GAA	AAUGGAAU	AUUCCAUUA	UGACAACA
20	3939	UAAUGACU	CUGAUGA	X	GAA	AUUCCUGC	GCAGGAAUC	AGUCAUUA
	3943	GAGAUAAU	CUGAUGA	X	GAA	ACUGAUUC	GAAUCAGUC	AUUAUCUC
	3946	CUGGAGAU	CUGAUGA	X	GAA	AUGACUGA	UCAGUCAUU	AUCUCCAG
	3947	UCUGGAGA	CUGAUGA	X	GAA	AAUGACUG	CAGUCAUUA	UCUCCAGA
	3949	GUUCUGGA	CUGAUGA	X	GAA	AUAAUGAC	GUCAUUAUC	UCCAGAAC
25	3951	CUGUUCUG	CUGAUGA	X	GAA	AGAUAAUG	CAUUAUCUC	CAGAACAG
	3961	CUUUCGCU	CUGAUGA	X	GAA	ACUGUUCU	AGAACAGUA	AGCGAAAG
	3987	AAUGUUUU	CUGAUGA	X	GAA	ACACUCAC	GUGAGUGUA	AAAACAUU
	3995	UAUCUUCA	CUGAUGA	X	GAA	AUGUUUUU	AAAAACAUU	UGAAGAUA
	3996	AUAUCUUC	CUGAUGA	X	GAA	AAUGUUUU	AAAACAUUU	GAAGAUAU
30	4003	CAAUGGGA	CUGAUGA	X	GAA	AUCUUCAA	UUGAAGAUA	UCCCAUUG

	4005	UCCAAUGG	CUGAUGA	X	GAA	AUAUCUUC	GAAGAUAUC C	CAUUGGA
	4010	GUUCCUCC	CUGAUGA	X	GAA	AUGGGAUA	UAUCCCAUU G	GAGGAAC
	4026	AUCACUUU	CUGAUGA	X	GAA	ACUUCUGG	CCAGAAGUA A	AAGUGAU
	4035	UCAUCUGG	CUGAUGA	X	GAA	AUCACUUU	AAAGUGAUC CO	CAGAUGA
5	4068	GAUGCAAG	CUGAUGA	X	GAA	ACCAUCCC	GGGAUGGUC C	UUGCAUC
	4071	UCUGAUGC	CUGAUGA	X	GAA	AGGACCAU	AUGGUCCUU GO	CAUCAGA
	4076	GCUCUUCU	CUGAUGA	X	GAA	AUGCAAGG	CCUUGCAUC AG	GAAGAGC
	4093	GUCUUCCA	CUGAUGA	X	GAA	AGUUUUCA	UGAAAACUC U	GGAAGAC
	4112	AUGGAGAU	CUGAUGA	X	GAA	AUUUGUUC	GAACAAAUU A	UCUCCAU
10	4113	GAUGGAGA	CUGAUGA	X	GAA	AAUUUGUU	AACAAAUUA U	CUCCAUC
	4115	AAGAUGGA	CUGAUGA	X	GAA	AUAAUUUG	CAAAUUAUC U	CCAUCUU
	4117	AAAAGAUG	CUGAUGA	X	GAA	AGAUAAUU	AAUUAUCUC CA	AUCUUUU
	4121	CACCAAAA	CUGAUGA	X	GAA	AUGGAGAU	AUCUCCAUC UT	JUUGGUG
	4123	UCCACCAA	CUGAUGA	X	GAA	AGAUGGAG	CUCCAUCUU U	JGGUGGA
15	4124	UUCCACCA	CUGAUGA	X	GAA	AAGAUGGA	UCCAUCUUU UC	GGUGGAA
	4125	AUUCCACC	CUGAUGA	X	GAA	AAAGAUGG	CCAUCUUUU GO	GUGGAAU
	4144	CCUGCUUU	CUGAUGA	X	GAA	ACUGGGCA	UGCCCAGUA AA	AAGCAGG
	4157	AGGCCACA	CUGAUGA	X	GAA	ACUCCCUG	CAGGGAGUC UC	GUGGCCU
	4166	AGCCUUCC	CUGAUGA	X	GAA	AGGCCACA	UGUGGCCUC GC	GAAGGCU
20	4175	UCUGGUUG	CUGAUGA	X	GAA	AGCCUUCC	GGAAGGCUC CA	AACCAGA
	4193	CAGACUGG	CUGAUGA	X	GAA	AGCCACUG	CAGUGGCUA CO	CAGUCUG
	4199	GAUACCCA	CUGAUGA	X	GAA	ACUGGUAG	CUACCAGUC UC	GGUAUC
	4205	CUGAGUGA	CUGAUGA	X	GAA	ACCCAGAC	GUCUGGGUA UC	CACUCAG
	4207	AUCUGAGU	CUGAUGA	X	GAA	AUACCCAG	CUGGGUAUC AC	CUCAGAU
25	4211	UGUCAUCU	CUGAUGA	X	GAA	AGUGAUAC	GUAUCACUC AG	GAUGACA
	4235	CGCUGGAG	CUGAUGA	X	GAA	ACACGGUG	CACCGUGUA CU	JCCAGCG
	4238	CGUCGCUG	CUGAUGA	X	GAA	AGUACACG	CGUGUACUC CA	AGCGACG
	4257	AUCUUUAA	CUGAUGA	X	GAA	AGUCCUGC	GCAGGACUU UU	JAAAGAU
	4258	CAUCUUUA	CUGAUGA	X	GAA	AAGUCCUG	CAGGACUUU UA	AAGAUG
30	4259	CCAUCUUU	CUGAUGA	x	GAA	AAAGUCCU	AGGACUUUU AA	AGAUGG

	4260	ACCAUCUU	CUGAUGA	X	GAA	AAAAGUCC	GGACUUUUA	AAGAUGGU
	4281	UCAGCGUG	CUGAUGA	X	GAA	ACUGCAGC	GCUGCAGUU	CACGCUGA
	4282	GUCAGCGU	CUGAUGA	X	GAA	AACUGCAG	CUGCAGUUC	ACGCUGAC
	4292	UGGUCCCU	CUGAUGA	X	GAA	AGUCAGCG	CGCUGACUC	AGGGACCA
5	4311	CAGGAGGU	CUGAUGA	X	GAA	AGCUGCAG	CUGCAGCUC	ACCUCCUG
	4316	UUAAACAG	CUGAUGA	X	GAA	AGGUGAGC	GCUCACCUC	CUGUUUAA
	4321	UCCAUUUA	CUGAUGA	X	GAA	ACAGGAGG	CCUCCUGUU	UAAAUGGA
	4322	UUCCAUUU	CUGAUGA	X	GAA	AACAGGAG	CUCCUGUUU	AAAUGGAA
	4323	CUUCCAUU	CUGAUGA	X	GAA	AAACAGGA	UCCUGUUUA	AAUGGAAG
10	4336	CGGGACAG	CUGAUGA	X	GAA	ACCACUUC	GAAGUGGUC	CUGUCCCG
	4341	GGAGCCGG	CUGAUGA	X	GAA	ACAGGACC	GGUCCUGUC	CCGGCUCC
	4348	UGGGGGCG	CUGAUGA	X	GAA	AGCCGGGA	UCCCGGCUC	CGCCCCCA
	4360	AUUUCCAG	CUGAUGA	X	GAA	AGUUGGGG	CCCCAACUC	CUGGAAAU
	4369	UCUCUCGU	CUGAUGA	X	GAA	AUUUCCAG	CUGGAAAUC	ACGAGAGA
15	4387	GAAAAUCU	CUGAUGA	X	GAA	AGCAGCAC	GUGCUGCUU	AGAUUUUC
	4388	UGAAAAUC	CUGAUGA	X	GAA	AAGCAGCA	UGCUGCUUA	GAUUUUCA
	4392	CACUUGAA	CUGAUGA	X	GAA	AUCUAAGC	GCUUAGAUU	UUCAAGUG
	4393	ACACUUGA	CUGAUGA	X	GAA	AAUCUAAG	CUUAGAUUU	UCAAGUGU
	4394	AACACUUG	CUGAUGA	X	GAA	AAAUCUAA	UUAGAUUUU	CAAGUGUU
20	4395	CAACACUU	CUGAUGA	X	GAA	AAAAUCUA	UAGAUUUUC	AAGUGUUG
	4402	GAAAGAAC	CUGAUGA	X	GAA	ACACUUGA	UCAAGUGUU	GUUCUUUC
	4405	GUGGAAAG	CUGAUGA	X	GAA	ACAACACU	AGUGUUGUU	CUUUCCAC
	4406	GGUGGAAA	CUGAUGA	X	GAA	AACAACAC	GUGUUGUUC	UUUCCACC
	4408	GUGGUGGA	CUGAUGA	X	GAA	AGAACAAC	GUUGUUCUU	UCCACCAC
25	4409	GGUGGUGG	CUGAUGA	X	GAA	AAGAACAA	UUGUUCUUU	CCACCACC
	4410	GGGUGGUG	CUGAUGA	X	GAA	AAAGAACA	UGUUCUUUC	CACCACCC
	4425	AAUGUGGC	CUGAUGA	X	GAA	ACUUCCGG	CCGGAAGUA	GCCACAUU
	4433	GAAAAUCA	CUGAUGA	X	GAA	AUGUGGCU	AGCCACAUU	UGAUUUUC
	4434	UGAAAAUC	CUGAUGA	X	GAA	AAUGUGGC	GCCACAUUU	GAUUUUCA
30	4438	AAAAUGAA	CUGAUGA	Х	GAA	AUCAAAUG	CAUUUGAUU	UUCAUUUU

	4439	AAAAAUGA	CUGAUGA	x	GAA	AAUCAAAU	AUUUGAUUU	UCAUUUUU
	4440	CAAAAAUG	CUGAUGA	X	GAA	AAAUCAAA	UUUGAUUUU	CAUUUUUG
	4441	CCAAAAAU	CUGAUGA	X	GAA	AAAAUCAA	UUGAUUUUC	AUUUUUGG
	4444	CCUCCAAA	CUGAUGA	X	GAA	AUGAAAAU	AUUUUCAUU	UUUGGAGG
5	4445	UCCUCCAA	CUGAUGA	X	GAA	AAUGAAAA	UUUUCAUUU	UUGGAGGA
	4446	CUCCUCCA	CUGAUGA	X	GAA	AAAUGAAA	UUUCAUUUU	UGGAGGAG
	4447	ccuccucc	CUGAUGA	X	GAA	AAAAUGAA	UUCAUUUUU	GGAGGAGG
	4461	UGCAGUCU	CUGAUGA	X	GAA	AGGUCCCU	AGGGACCUC	AGACUGCA
	4477	CUGAGGAC	CUGAUGA	X	GAA	AGCUCCUU	AAGGAGCUU	GUCCUCAG
10	4480	GCCCUGAG	CUGAUGA	X	GAA	ACAAGCUC	GAGCUUGUC	CUCAGGGC
	4483	AAUGCCCU	CUGAUGA	Х	GAA	AGGACAAG	CUUGUCCUC	AGGGCAUU
	4491	UCUCUGGA	CUGAUGA	X	GAA	AUGCCCUG	CAGGGCAUU	UCCAGAGA
	4492	UUCUCUGG	CUGAUGA	X	GAA	AAUGCCCU	AGGGCAUUU	CCAGAGAA
	4493	CUUCUCUG	CUGAUGA	X	GAA	AAAUGCCC	GGGCAUUUC	CAGAGAAG
15	4525	GUAGAGUC	CUGAUGA	X	GAA	ACACAUUC	GAAUGUGUU	GACUCUAC
	4530	AGAGAGUA	CUGAUGA	X	GAA	AGUCAACA	UGUUGACUC	UACUCUCU
	4532	AAAGAGAG	CUGAUGA	X	GAA	AGAGUCAA	UUGACUCUA	CUCUCUUU
	4535	GGAAAAGA	CUGAUGA	X	GAA	AGUAGAGU	ACUCUACUC	UCUUUUCC
	4537	AUGGAAAA	CUGAUGA	X	GAA	AGAGUAGA	UCUACUCUC	UUUUCCAU
20	4539	GAAUGGAA	CUGAUGA	X	GAA	AGAGAGUA	UACUCUCUU	UUCCAUUC
	4540	UGAAUGGA	CUGAUGA	X	GAA	AAGAGAGU	ACUCUCUUU	UCCAUUCA
	4541	AUGAAUGG	CUGAUGA	X	GAA	AAAGAGAG	CUCUCUUUU	CCAUUCAU
	4542	AAUGAAUG	CUGAUGA	X	GAA	AAAAGAGA	UCUCUUUUC	CAUUCAUU
	4546	UUUAAAUG	CUGAUGA	X	GAA	AUGGAAAA	UUUUCCAUU	CAUUUAAA
25	4547	UAAAU	CUGAUGA	X	GAA	AAUGGAAA	UUUCCAUUC	AAAAUUUA
	4550	GACUUUUA	CUGAUGA	X	GAA	AUGAAUGG	CCAUUCAUU	UAAAAGUC
	4551	GGACUUUU	CUGAUGA	X	GAA	AAUGAAUG	CAUUCAUUU	AAAAGUCC
	4552	AGGACUUU	CUGAUGA	X	GAA	AAAUGAAU	AUUCAUUUA	AAAGUCCU
	4558	UUAUAUAG	CUGAUGA	X	GAA	ACUUUUAA	UUAAAAGUC	CUAUAUAA
30	4561	ACAUUAUA	CUGAUGA	X	GAA	AGGACUUU	AAAGUCCUA	UAUAAUGU

	4563	GCACAUUA	CUGAUGA	Х	GAA	AUAGGACU	AGUCCUAUA	. UAAUGUG(
	4565	GGGCACAU	CUGAUGA	X	GAA	AUAUAGGA	UCCUAUAUA	AUGUGCC
	4583	GGUAGUGA	CUGAUGA	X	GAA	ACCACAGC	GCUGUGGUC	UCACUACO
	4585	CUGGUAGU	CUGAUGA	X	GAA	AGACCACA	UGUGGUCUC	ACUACCAC
5	4589	UUAACUGG	CUGAUGA	X	GAA	AGUGAGAC	GUCUCACUA	CCAGUUAA
	4595	UUUGCUUU	CUGAUGA	X	GAA	ACUGGUAG	CUACCAGUU	AAAGCAAA
	4596	UUUUGCUU	CUGAUGA	X	GAA	AACUGGUA	UACCAGUUA	AAGCAAAA
	4609	GUGUUUGA	CUGAUGA	X	GAA	AGUCUUUU	AAAAGACUU	UCAAACAC
	4610	CGUGUUUG	CUGAUGA	X	GAA	AAGUCUUU	AAAGACUUU	CAAACACG
10	4611	ACGUGUUU	CUGAUGA	X	GAA	AAAGUCUU	AAGACUUUC	AAACACGU
	4625	GGAGGACA	CUGAUGA	X	GAA	AGUCCACG	CGUGGACUC	UGUCCUCO
	4629	UCUUGGAG	CUGAUGA	X	GAA	ACAGAGUC	GACUCUGUC	CUCCAAGA
	4632	ACUUCUUG	CUGAUGA	X	GAA	AGGACAGA	UCUGUCCUC	CAAGAAGU
	4654	GUUUCACA	CUGAUGA	X	GAA	AGGUGCCG	CGGCACCUC	UGUGAAAC
15	4668	GCCCAUUC	CUGAUGA	X	GAA	AUCCAGUU	AACUGGAUC	GAAUGGGC
	4683	AACACACA	CUGAUGA	X	GAA	AGCAUUGC	GCAAUGCUU	UGUGUGUU
	4684	CAACACAC	CUGAUGA	X	GAA	AAGCAUUG	CAAUGCUUU	GUGUGUUG
	4691	CCAUCCUC	CUGAUGA	X	GAA	ACACACAA	UUGUGUGUU	GAGGAUGG
	4709	GGCCCUGG	CUGAUGA	X	GAA	ACAUCUCA	UGAGAUGUC	CCAGGGCC
20	4722	GGUAGACA	CUGAUGA	X	GAA	ACUCGGCC	GGCCGAGUC	UGUCUACC
	4726	CCAAGGUA	CUGAUGA	X	GAA	ACAGACUC	GAGUCUGUC	UACCUUGG
	4728	CUCCAAGG	CUGAUGA	X	GAA	AGACAGAC	GUCUGUCUA	CCUUGGAG
	4732	AAGCCUCC	CUGAUGA	X	GAA	AGGUAGAC	GUCUACCUU	GGAGGCUU
	4740	CCUCCACA	CUGAUGA	X	GAA	AGCCUCCA	UGGAGGCUU	UGUGGAGG
25	4741	UCCUCCAC	CUGAUGA	X	GAA	AAGCCUCC	GGAGGCUUU	GUGGAGGA
	4758	UUGGCUCA	CUGAUGA	X	GAA	AGCCCGCA	UGCGGGCUA	UGAGCCAA
	4771	CCACACUU	CUGAUGA	X	GAA	ACACUUGG	CCAAGUGUU	AAGUGUGG
	4772	CCCACACU	CUGAUGA	X	GAA	AACACUUG	CAAGUGUUA	AGUGUGGG
	4811	CUCCGAGC	CUGAUGA	X	GAA	ACUUGCGC	GCGCAAGUC	GCUCGGAG
30	4815	CGCUCUCC	CUGAUGA	х	GAA	AGCGACUU	AAGUCGCUC	GGAGAGCG

	4826	CAGGCUCC	CUGAUGA	X	GAA	ACCGCUCU	AGAGCGGUU	GGAGCCUG
	4844	GCCAGCAC	CUGAUGA	X	GAA	AUGCAUCU	AGAUGCAUU	GUGCUGGC
	4854	CUCCACCA	CUGAUGA	X	GAA	AGCCAGCA	UGCUGGCUC	UGGUGGAG
	4870	CAGGCCAC	CUGAUGA	X	GAA	AGCCCACC	GGUGGGCUU	GUGGCCUG
5	4880	CGUUUCCU	CUGAUGA	X	GAA	ACAGGCCA	UGGCCUGUC	AGGAAACG
	4908	CAAAACCA	CUGAUGA	X	GAA	ACCCUGCC	GGCAGGGUU	UGGUUUUG
	4909	CCAAAACC	CUGAUGA	X	GAA	AACCCUGC	GCAGGGUUU	GGUUUUGG
	4913	CCUUCCAA	CUGAUGA	X	GAA	ACCAAACC	GGUUUGGUU	UUGGAAGG
	4914	ACCUUCCA	CUGAUGA	X	GAA	AACCAAAC	GUUUGGUUU	UGGAAGGU
10	4915	AACCUUCC	CUGAUGA	X	GAA	AAACCAAA	UUUGGUUUU	GGAAGGUU
	4923	AGCACGCA	CUGAUGA	x	GAA	ACCUUCCA	UGGAAGGUU	UGCGUGCU
	4924	GAGCACGC	CUGAUGA	X	GAA	AACCUUCC	GGAAGGUUU	GCGUGCUC
	4932	ACUGUGAA	CUGAUGA	X	GAA	AGCACGCA	UGCGUGCUC	UUCACAGU
	4934	CGACUGUG	CUGAUGA	x	GAA	AGAGCACG	CGUGCUCUU	CACAGUCG
15	4935	CCGACUGU	CUGAUGA	X	GAA	AAGAGCAC	GUGCUCUUC	ACAGUCGG
	4941	UGUAACCC	CUGAUGA	X	GAA	ACUGUGAA	UUCACAGUC	GGGUUACA
	4946	UCGCCUGU	CUGAUGA	X	GAA	ACCCGACU	AGUCGGGUU	ACAGGCGA
	4947	CUCGCCUG	CUGAUGA	X	GAA	AACCCGAC	GUCGGGUUA	CAGGCGAG
	4957	CCACAGGG	CUGAUGA	X	GAA	ACUCGCCU	AGGCGAGUU	CCCUGUGG
20	4958	GCCACAGG	CUGAUGA	X	GAA	AACUCGCC	GGCGAGUUC	CCUGUGGC
	4969	GAGUAGGA	CUGAUGA	X	GAA	ACGCCACA	UGUGGCGUU	UCCUACUC
	4970	GGAGUAGG	CUGAUGA	X	GAA	AACGCCAC	GUGGCGUUU	CCUACUCC
	4971	AGGAGUAG	CUGAUGA	X	GAA	AAACGCCA	UGGCGUUUC	CUACUCCU
	4974	AUUAGGAG	CUGAUGA	X	GAA	AGGAAACG	CGUUUCCUA	CUCCUAAU
25	4977	CUCAUUAG	CUGAUGA	X	GAA	AGUAGGAA	UUCCUACUC	CUAAUGAG
	4980	ACUCUCAU	CUGAUGA	X	GAA	AGGAGUAG	CUACUCCUA	AUGAGAGU
	4989	CCGGAAGG	CUGAUGA	X	GAA	ACUCUCAU	AUGAGAGUU	CCUUCCGG
	4990	UCCGGAAG	CUGAUGA	X	GAA	AACUCUCA	UGAGAGUUC	CUUCCGGA
	4993	GAGUCCGG	CUGAUGA	X	GAA	AGGAACUC	GAGUUCCUU	CCGGACUC
30	4994	AGAGUCCG	CUGAUGA	x	GAA	AAGGAACU	AGUUCCUUC	CGGACUCU

	5001	ACACGUAA	CUGAUGA	X	GAA	AGUCCGGA	UCCGGACUC UUACGUGU
	5003	AGACACGU	CUGAUGA	X	GAA	AGAGUCCG	CGGACUCUU ACGUGUCU
	5004	GAGACACG	CUGAUGA	X	GAA	AAGAGUCC	GGACUCUUA CGUGUCUC
	5010	GGCCAGGA	CUGAUGA	X	GAA	ACACGUAA	UUACGUGUC UCCUGGCC
5	5012	CAGGCCAG	CUGAUGA	X	GAA	AGACACGU	ACGUGUCUC CUGGCCUG
	5046	GAAGGAGC	CUGAUGA	X	GAA	AGCUGCAU	AUGCAGCUU GCUCCUUC
	5050	UGAGGAAG	CUGAUGA	X	GAA	AGCAAGCU	AGCUUGCUC CUUCCUCA
	5053	AGAUGAGG	CUGAUGA	X	GAA	AGGAGCAA	UUGCUCCUU CCUCAUCU
	5054	GAGAUGAG	CUGAUGA	X	GAA	AAGGAGCA	UGCUCCUUC CUCAUCUC
10	5057	UGAGAGAU	CUGAUGA	X	GAA	AGGAAGGA	UCCUUCCUC AUCUCUCA
	5060	GCCUGAGA	CUGAUGA	X	GAA	AUGAGGAA	UUCCUCAUC UCUCAGGC
	5062	CAGCCUGA	CUGAUGA	X	GAA	AGAUGAGG	CCUCAUCUC UCAGGCUG
	5064	CACAGCCU	CUGAUGA	X	GAA	AGAGAUGA	UCAUCUCUC AGGCUGUG
	5076	UCUGAAUU	CUGAUGA	X	GAA	AGGCACAG	CUGUGCCUU AAUUCAGA
15	5077	UUCUGAAU	CUGAUGA	X	GAA	AAGGCACA	UGUGCCUUA AUUCAGAA
	5080	GUGUUCUG	CUGAUGA	X	GAA	AUUAAGGC	GCCUUAAUU CAGAACAC
	5081	GGUGUUCU	CUGAUGA	X	GAA	AAUUAAGG	CCUUAAUUC AGAACACC
	5105	CCUCUGCC	CUGAUGA	X	GAA	ACGUUCCU	AGGAACGUC GGCAGAGG
	5116	CCCGUCAG	CUGAUGA	X	GAA	AGCCUCUG	CAGAGGCUC CUGACGGG
20	5135	GUUCUCAC	CUGAUGA	Х	GAA	AUUCUUCG	CGAAGAAUU GUGAGAAC
	5156	GAAACCCU	CUGAUGA	X	GAA	AGUUUCUG	CAGAAACUC AGGGUUUC
	5162	CCAGCAGA	CUGAUGA	X	GAA	ACCCUGAG	CUCAGGGUU UCUGCUGG
	51 63	CCCAGCAG	CUGAUGA	X	GAA	AACCCUGA	UCAGGGUUU CUGCUGGG
	5164	ACCCAGCA	CUGAUGA	X	GAA	AAACCCUG	CAGGGUUUC UGCUGGGU
25	52 03	AACCCUCA	CUGAUGA	X	GAA	ACCUGCCA	UGGCAGGUC UGAGGGUU
	5211	UGACAGAG	CUGAUGA	X	GAA	ACCCUCAG	CUGAGGGUU CUCUGUCA
	5212	UUGACAGA	CUGAUGA	X	GAA	AACCCUCA	UGAGGGUUC UCUGUCAA
	5214	ACUUGACA	CUGAUGA	X	GAA	AGAACCCU	AGGGUUCUC UGUCAAGU
	5218	CGCCACUU	CUGAUGA	X	GAA	ACAGAGAA	UUCUCUGUC AAGUGGCG
30	5229	UGAGCCUU	CUGAUGA	X	GAA	ACCGCCAC	GUGGCGGUA AAGGCUCA

PCT/US96/17480

WO 97/15662

	5236	ACCAGCCU	CUGAUGA	х	GAA	AGCCUUUA	UAAAGGCUC	AGGCUGGU
	5247	AGAGGAAG	CUGAUGA	х	GAA	ACACCAGC	GCUGGUGUU	CUUCCUCU
	5248	UAGAGGAA	CUGAUGA	х	GAA	AACACCAG	CUGGUGUUC	UUCCUCUA
	5250	GAUAGAGG	CUGAUGA	х	GAA	AGAACACC	GGUGUUCUU	CCUCUAUC
5						AAGAACAC	GUGUUCUUC	CUCUAUCU
						AGGAAGAA	UUCUUCCUC	
						AGAGGAAG	CUUCCUCUA	
	5258	GGAGUGGA	CUGAUGA	X	GAA	AUAGAGGA	UCCUCUAUC	
						AGAUAGAG	CUCUAUCUC	
10						AGUGGAGA	UCUCCACUC	
						ACAGGAGU	ACUCCUGUC	
						ACUUGGGG	CCCCAAGUC	
						AGGACUUG	CAAGUCCUC	
	5290	AGCUAAAA	CUGAUGA	X	GAA	ACUGAGGA	UCCUCAGUA	
15						AUACUGAG	CUCAGUAUU	
						AAUACUGA	UCAGUAUUU	
						AAAUACUG	CAGUAUUUU	
						AAAAUACU	AGUAUUUUA	
						AGCUAAAA	UUUUAGCUU	
20						AAGCUAAA	UUUAGCUUU	
	5307	CCAUCAGG	CUGAUGA	Х	GAA	AGCCACAA	UUGUGGCUU	
	5308	GCCAUCAG	CUGAUGA	Х	GAA	AAGCCACA	UGUGGCUUC	CUGAUGGC
							AGAAAAAUC	
	5327	AACCAAUU	CUGAUGA	х	GAA	AGAUUUUU	AAAAAUCUU	AAUUGGUU
25	5328	CAACCAAU	CUGAUGA	х	GAA	AAGAUUUU	AAAAUCUUA	AUUGGUUG
	5331	AACCAACC	CUGAUGA	х	GAA	AUUAAGAU	AUCUUAAUU	GGUUGGUU
	5335	AGCAAACC	CUGAUGA	X	GAA	ACCAAUUA	UAAUUGGUU	GGUUUGCU
							UGGUUGGUU	
							GGUUGGUUU	
30							GGUUUGCUC	

	5346	AUUAUCUG	CUGAUGA	X	GAA	AGAGCAAA	UUUGCUCUC	CAGAUAAU
	5352	CUAGUGAU	CUGAUGA	X	GAA	AUCUGGAG	CUCCAGAUA	AUCACUAG
	5355	UGGCUAGU	CUGAUGA	X	GAA	AUUAUCUG	CAGAUAAUC	ACUAGCCA
	5359	AAUCUGGC	CUGAUGA	X	GAA	AGUGAUUA	UAAUCACUA	GCCAGAUU
5	5367	AAUUUCGA	CUGAUGA	X	GAA	AUCUGGCU	AGCCAGAUU	UCGAAAUU
	5368	UAAUUUCG	CUGAUGA	X	GAA	AAUCUGGC	GCCAGAUUU	CGAAAUUA
	5369	GUAAUUUC	CUGAUGA	X	GAA	AAAUCUGG	CCAGAUUUC	GAAAUUAC
	5375	UAAAAAGU	CUGAUGA	X	GAA	AUUUCGAA	UUCGAAAUU	ACUUUUUA
	5376	CUAAAAAG	CUGAUGA	X	GAA	AAUUUCGA	UCGAAAUUA	CUUUUUAG
10	5379	CGGCUAAA	CUGAUGA	X	GAA	AGUAAUUU	AAAUUACUU	UUUAGCCG
	5380	UCGGCUAA	CUGAUGA	X	GAA	AAGUAAUU	AAUUACUUU	UUAGCCGA
	5381	CUCGGCUA	CUGAUGA	X	GAA	AAAGUAAU	AUUACUUUU	UAGCCGAG
	5382	CCUCGGCU	CUGAUGA	X	GAA	AAAAGUAA	UUACUUUUU	AGCCGAGG
	5383	ACCUCGGC	CUGAUGA	X	GAA	AAAAAGUA	UACUUUUUA	GCCGAGGU
15	5392	GUUAUCAU	CUGAUGA	X	GAA	ACCUCGGC	GCCGAGGUU	AUGAUAAC
	5393	UGUUAUCA	CUGAUGA	X	GAA	AACCUCGG	CCGAGGUUA	UGAUAACA
	5398	GUAGAUGU	CUGAUGA	X	GAA	AUCAUAAC	GUUAUGAUA	ACAUCUAC
	5403	AUACAGUA	CUGAUGA	X	GAA	AUGUUAUC	GAUAACAUC	UACUGUAU
	5405	GGAUACAG	CUGAUGA	X	GAA	AGAUGUUA	UAACAUCUA	CUGUAUCC
20	5410	CUAAAGGA	CUGAUGA	X	GAA	ACAGUAGA	UCUACUGUA	UCCUUUAG
	5412	UUCUAAAG	CUGAUGA	X	GAA	AUACAGUA	UACUGUAUC	CUUUAGAA
	5415	AAAUUCUA	CUGAUGA	X	GAA	AGGAUACA	UGUAUCCUU	UAGAAUUU
	5416	AAAAUUCU	CUGAUGA	X	GAA	AAGGAUAC	GUAUCCUUU	AGAAUUUU
	5417	UAAAAUUC	CUGAUGA	X	GAA	AAAGGAUA	UAUCCUUUA	GAAUUUUA
25							UUUAGAAUU	
							UUAGAAUUU	
							UAGAAUUUU	
							AGAAUUUUA	
							UUUAACCUA	
30	5432	CAUAGUUU	CUGAUGA	X	GAA	AUAGGUUA	UAACCUAUA	AAACUAUG

PCT/US96/17480

149

5438 AGUAGACA CUGAUGA X GAA AGUUUUAU AUAAAACUA UGUCUACU
5442 AACCAGUA CUGAUGA X GAA ACAUAGUU AACUAUGUC UACUGGUU
5444 GAAACCAG CUGAUGA X GAA AGACAUAG CUAUGUCUA CUGGUUUC
5450 CAGGCAGA CUGAUGA X GAA ACCAGUAG CUACUGGUU UCUGCCUG
5451 ACAGGCAG CUGAUGA X GAA AACCAGUA UACUGGUUU CUGCCUGU
5452 CACAGGCA CUGAUGA X GAA AAACCAGU ACUGGUUUC UGCCUGUG

Where "X" represents stem II region of a HH ribozyme (Hertel et al., 1992 Nucleic Acids Res. 20 3252). The length of stem II may be \geq 2 base-pairs.

Table VII: Mouse flk-1 VEGF Receptor-Hairpin Ribozyme and Substrate Sequences

	ţ		up biboramo compos	, t
	Posi-			Sabstrace
	tion			
2	74	GGGACACA AGAA G	GGGACACA AGAA GGGCCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	GGGCCCA GAC UGUGUCCC
	88	GUUAUCCC AGAA G	GUUAUCCC AGAA GCGGGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UCCCGCA GCC GGGAUAAC
	105	GGAAUCGG AGAA G	GGAAUCGG AGAA GCCAGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	ceuggen gae eegaunee
	110	UCCGCGGA AGAA GGUCAG	GUCAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CUGACCC GAU UCCGCGGA
	125	CGGCUGUC AGAA GI	CGGCUGUC AGAA GUGUCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GGACACC GCU GACAGCCG
10	132	CCAGCCGC AGAA GI	CCAGCCGC AGAA GUCAGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GCUGACA GCC GCGGCUGG
	138	CUGGCUCC AGAA GO	CUGGCUCC AGAA GCGGCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AGCCGCG GCU GGAGCCAG
	175	CAGCGCAA AGAA GC	CAGCGCAA AGAA GGGGAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	cucccce enc mececne
	199	GUCACAGA AGAA GI	GUCACAGA AGAA GUAUGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	ccauacc ecc ucueugac
	309	CACAGAGC AGAA GO	CACAGAGC AGAA GCUAGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GCUAGCU GUC GCUCUGUG
15	342	CCCACAGA AGAA GO	CCCACAGA AGAA GCUCGG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	CCGAGCC GCC UCUGUGGG
	434	UGCAAGUA AGAA GA	UGCAAGUA AGAA GAAGGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CCCUUCA GAU UACUUGCA
	630	UAGACAUA AGAA GI	UAGACAUA AGAA GUGGAG ACCAGAGAAACACGCUGGUGGGACAUUACCUGGUA	CUCCACU GUU UAUGUCUA
	655	GAAUGGUG AGAA GL	GAAUGGUG AGAA GUAAUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GAUUACA GAU CACCAUUC
	739	CGACCCUC AGAA GC	CGACCCUC AGAA GGGGAU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA	AUCCCCU GCC GAGGGUCG

CGUUAAGC

GAC

UCCUACG

GUAGGA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA

AGAA

GCUUAACG

2639

151

151

GAU GGAAACAG GAAGCCU GCU CCUACAGA GCAACCU GCU GCCCAGCC GCC CAGCCAAC UGUCCCU GUU GUGCACUG CACAUGGG GUU UGCAAGAA CAAGAUAA CAUCAUCC GGAACCU GAC UAUCCGCA GUC UAUCAUGU GAU GAUCAAGA UVACCCA GCU CCUGAUAU GAU CGGUGAGA GAU UGAAGGAA GGAGAAAA AUGCACA GUC UACGCCAA UCCUACA GAC CCGGCCAA GAC GCN CCC ungenen gen ACCUGCU AACAUCG UGUUCCG AUGCCCU CACACCA UCAAACA CCUAUCA GCUAUCU GUGGACG CACCCCA GGUUGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUUUGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGUUCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CUGUUUCC AGAA GGAACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGUAA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGGGUG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUGCAU ACCAGAGAAACACGCUUGUGGGAACAUUACCUGGUA GGCUUC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA UUGGCCGG AGAA GUAGGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGCAU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GCAGGU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CAGUGCAC AGAA GGGACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAUGUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGUGUG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GAGCAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAUAGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAUAGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUCCAC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA AGAA UNAUCUUG AGAA AGAA AUAUCAGG AGAA UUGGCGUA AGAA AGAA GGCUGGGC AGAA AGAA UUCUUGCA AGAA UGCGGAUA AGAA ACAUGAUA AGAA AGAA UCUCACCG AGAA AGAA GGAUGAUG AGAA CCCAUGUG UCUGUAGG UUCCUUCA GUUGGCUG UCUUGAUC 1365 1629 1696 1796 1985 1556 1950 2055 2082 2208 1002 1229 1687 1953 2252 2444 920 807 10 15 ហ

GUU CACGCUGA

UGCUGCA

UCAGCGUG AGAA GCAGCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

4278

152

GGAUCCA GAU GAAUUGCC GCU GAAACUAG GCUUUUGG CUUGGAGC UGUUACA GCU UCCAAGUG UCUGCCA GCU CAGGCUUU GCU UGGCCCGG AGACCCG GAU UAUGUCAG GAC UCCCUTUG GGCUCCU GAC UACACUAC UGUACCA GAC CAUGCUGG CUGGACU GCU GGCAUGAG GCC UACCUCAC CUCACCU GUU UCCUGUAU GAUCCCA GAU GACAGCCA CAGUGGCU GCUACCA GUC UGGGUAUC GACACAGA GAC ACUUCCU GAC GAU GAC GGGACCG UGAGGCA GACUUCG GAUGCCC ncncccn CCAACCA UCACUCA GGCAAUUC AGAA GGAUCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CUAGUJUC AGAA GGUCCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GCCUCA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA SCUCCAAG AGAA GGAAGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGCAGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AGAA GUAACA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA CCGGGCCA AGAA GAAGUC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CUGACAUA AGAA GGGUCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CAAAGGGA AGAA GGCAUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGAGCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CCAGCAUG AGAA GGUACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUCCAG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUGAGGUA AGAA GGGAGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AUACAGGA AGAA GGUGAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGAUC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA AGCCACUG AGAA GGUUGG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGUAGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA UCUGUGUC AGAA GAGUGA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CCAAAAGC AGAA GUAGUGUA AGAA CUCAUGCC AGAA UGGCUGUC AGAA AGAA AGAA AAAGCCUG CACUUGGA GAUACCCA 2703 3278 2777 2832 3199 3450 3475 3304 3689 3421 3663 3703 3860 3873 4038 4196 4212 4181 10 Ŋ 15

PCT/US96/17480 WO 97/15662

153

CGGCUCC GCC CCCAACUC UCACGCU GAC UCAGGGAC CACUGCA GCU CACCUCCU CCGGCCCC veucces seu cesecee AGGUGCU GCU UAGAUUUU guececu ecu eugeueue CGAGUCU GUC UACCUUGG GAGAGCG GUU GGAGCCUG GGCUCCU GAC GGGGCCGA GGUUUCU GCU GGGUGGAG ACCUCCU GUU UAAAUGGA GACCUCA GAC UGCAAGGA GGACUCU GUC CUCCAAGA GCCUGCA GAU GCAUUGUG GGCAGGGU CUUCACA GUC GGGUUACA GAC UCUUACGU UGAUGCA GCU UGCUCCUU ggg nganaan ana AAAGGCG CCUUCCG GUCCCUGA AGAA GCGUGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCAGUG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGAGGU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGACCA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGGGGCGG AGAA GGGACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAGUUGGG AGAA GAGCCG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA AAAAUCUA AGAA GCACCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UCCUUGCA AGAA GAGGUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGCAC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA UCUUGGAG AGAA GAGUCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GACUCG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CAGGCUCC AGAA GCUCUC ACCAGAGAACACACGUUGUGUGGUACAUUACCUGGUA GCAGGC ACCAGAGAACACACGUUGUGGGAACAUUACCUGGUA ACCCUGCC AGAA GCCUUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUGAAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA ACGUAAGA AGAA GGAAGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AAGGAGCA AGAA GCAUCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UCGGCCCC AGAA GGAGCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CUCCACCC AGAA GAAACC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AGAA UGUAACCC AGAA AGAA AGAA GAGACCAC AGAA AGAA AGAA AGGAGGUG GGAGCCGG CCAAGGUA CACAAUGC UCCAUUUA 4349 4287 4307 4318 4338 4344 4383 4462 4626 4723 4823 4836 4896 4938 4996 5165 4574 5042 5118 10 15

ഗ

GCUUCCU GAU GGCAGAAA	CUAGCCA GAU UUCGAAAU	GGUTUCU GCC UGUGUGCU
UUUCUGCC AGAA GGAAGC ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA	AUUUCGAA AGAA GGCUAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	AGCACACA AGAA GAAACC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA
GGAAGC	GGCUAG	GAAACC
AGAA	AGAA	AGAA
ນນາດນອດດ	AUUUCGAA	AGCACACA
5310	5363	5453

155

Table VIII: Mouse flt-1 VEGF Receptor-Hammerhead Ribozyme and Substrate Sequence

	nt.	н	H Ribozy	me	Sec	puence	S	ubst	rate
	Posi-								
5	tion								
	17	GUGAGCAA	CUGAUGA	X	GAA	ACGCGGCC	GGCCGC	:GUC	UUGCUCAC
	19	UGGUGAGC	CUGAUGA	X	GAA	AGACGCGG	CCGCGU	ICUU	GCUCACCA
	23	ACCAUGGU	CUGAUGA	X	GAA	AGCAAGAC	GUCUUG	CUC	ACCAUGGU
	32	CAGCAGCU	CUGAUGA	X	GAA	ACCAUGGU	ACCAUG	GUC	AGCUGCUG
10	53	UAAGGCAA	CUGAUGA	X	GAA	ACCGCGGU	ACCGCG	GUC	UUGCCUUA
	55	CGUAAGGC	CUGAUGA	X	GAA	AGACCGCG	CGCGGU	ICUU	GCCUUACG
	60	CAGCGCGU	CUGAUGA	X	GAA	AGGCAAGA	UCUUGO	:כטט	ACGCGCUG
	61	GCAGCGCG	CUGAUGA	X	GAA	AAGGCAAG	CUUGCO	:UUA	CGCGCUGC
	71	AGACACCC	CUGAUGA	X	GAA	AGCAGCGC	GCGCUG	CUC	GGGUGUCU
15	78	GAGAAGCA	CUGAUGA	X	GAA	ACACCCGA	UCGGGU	IGUC	UGCUUCUC
	83	CCUGUGAG	CUGAUGA	X	GAA	AGCAGACA	UGUCUG	ເດດດ	CUCACAGG
	84	UCCUGUGA	CUGAUGA	X	GAA	AAGCAGAC	GUCUGO	:טטכ	UCACAGGA
	86	UAUCCUGU	CUGAUGA	X	GAA	AGAAGCAG	CUGCUU	ICUC	ACAGGAUA
	94	CUGAGCCA	CUGAUGA	X	GAA	AUCCUGUG	CACAGO	AUA	UGGCUCAG
20	100	UCGACCCU	CUGAUGA	X	GAA	AGCCAUAU	AUAUGG	CUC	AGGGUCGA
	106	UUAACUUC	CUGAUGA	X	GAA	ACCCUGAG	CUCAGO	GUC	GAAGUUAA
	112	GCACUUUU	CUGAUGA	X	GAA	ACUUCGAC	GUCGAA	'GUU	AAAAGUGC
	113	GGCACUUU	CUGAUGA	X	GAA	AACUUCGA	UCGAAG	AUU	AAAGUGCC
	132	GCCUUUUA	CUGAUGA	X	GAA	ACUCAGUU	AACUGA	GUU	UAAAAGGC
25	133	UGCCUUUU	CUGAUGA	X	GAA	AACUCAGU	ACUGAG	יטטט	AAAAGGCA
	134	GUGCCUUU	CUGAUGA	X	GAA	AAACUCAG	CUGAGU	IUUA	AAAGGCAC
	152	GCUUGCAU	CUGAUGA	X	GAA	ACAUGCUG	CAGCAU	IGUC	AUGCAAGC
	171	GAGAAAGA	CUGAUGA	X	GAA	AGUCUGGC	GCCAGA	CUC	UCUUUCUC
	173	UUGAGAAA	CUGAUGA	X	GAA	AGAGUCUG	CAGACU	ICUC	UUUCUCAA
30	175	ACUUGAGA	CUGAUGA	X	GAA	AGAGAGUC	GACUCU	ເດນດ	UCUCAAGU
	176	CACUUGAG	CUGAUGA	X	GAA	AAGAGAGU	ACUCUC	:ייייי	CUCAAGUG
	177	GCACUUGA	CUGAUGA	X	GAA	AAAGAGAG	cucucu	IUUC	UCAAGUGC

	179	CUGCACUU	CUGAUGA	X	GAA	AGAAAGAG	cucuuucuc	AAGUGCAG
	205	GAGACCAU	CUGAUGA	X	GAA	AGUGGGCU	AGCCCACUC	AUGGUCUC
	211	UGGGCAGA	CUGAUGA	X	GAA	ACCAUGAG	CUCAUGGUC	UCUGCCCA
	213	CGUGGGCA	CUGAUGA	X	GAA	AGACCAUG	CAUGGUCUC	UGCCCACG
5	254	GGGGGAGU	CUGAUGA	X	GAA	AUGCUCAG	CUGAGCAUC	ACUCCCCC
	258	CGAUGGGG	CUGAUGA	X	GAA	AGUGAUGC	GCAUCACUC	CCCCAUCG
	26 5	CACAGGCC	CUGAUGA	X	GAA	AUGGGGGA	UCCCCCAUC	GGCCUGUG
	282	UUGCCUGU	CUGAUGA	X	GAA	AUCCCUCC	GGAGGGAUA	ACAGGCAA
	29 2	UGCUGCAG	CUGAUGA	X	GAA	AUUGCCUG	CAGGCAAUU	CUGCAGCA
10	29 3	GUGCUGCA	CUGAUGA	X	GAA	AAUUGCCU	AGGCAAUUC	UGCAGCAC
	304	CCAAGGUC	CUGAUGA	X	GAA	AGGUGCUG	CAGCACCUU	GACCUUGG
	310	CCGUGUCC	CUGAUGA	X	GAA	AGGUCAAG	CUUGACCUU	GGACACGG
	341	CAGGUGUA	CUGAUGA	X	GAA	AGGCCCGU	ACGGGCCUC	UACACCUG
	343	UACAGGUG	CUGAUGA	X	GAA	AGAGGCCC	GGGCCUCUA	CACCUGUA
15	351	GAGGUAUC	CUGAUGA	X	GAA	ACAGGUGU	ACACCUGUA	GAUACCUC
	355	UAGGGAGG	CUGAUGA	X	GAA	AUCUACAG	CUGUAGAUA	CCUCCCUA
	359	GAUGUAGG	CUGAUGA	X	GAA	AGGUAUCU	AGAUACCUC	CCUACAUC
	363	AGUAGAUG	CUGAUGA	X	GAA	AGGGAGGU	ACCUCCCUA	CAUCUACU
	367	UCGAAGUA	CUGAUGA	X	GAA	AUGUAGGG	CCCUACAUC	UACUUCGA
20	36 9	CUUCGAAG	CUGAUGA	X	GAA	AGAUGUAG	CUACAUCUA	CUUCGAAG
	372	UUUCUUCG	CUGAUGA	X	GAA	AGUAGAUG	CAUCUACUU	CGAAGAAA
	37 3	UUUUCUUC	CUGAUGA	X	GAA	AAGUAGAU	AUCUACUUC	GAAGAAAA
	394	AGAUUGAA	CUGAUGA	X	GAA	AUUCCGCU	AGCGGAAUC	UUCAAUCU
	396	GUAGAUUG	CUGAUGA	X	GAA	AGAUUCCG	CGGAAUCUU	CAAUCUAC
25	397	UGUAGAUU	CUGAUGA	X	GAA	AAGAUUCC	GGAAUCUUC	AAUCUACA
	401	AAUAUGUA	CUGAUGA	X	GAA	AUUGAAGA	UCUUCAAUC	UACAUAUU
	403	CAAAUAUG	CUGAUGA	X	GAA	AGAUUGAA	UUCAAUCUA	CAUAUUUG
	407	CUAACAAA	CUGAUGA	X	GAA	AUGUAGAU	AUCUACAUA	UUUGUUAG
	409	CACUAACA	CUGAUGA	X	GAA	AUAUGUAG	CUACAUAUU	UGUUAGUG
30	410	UCACUAAC	CUGAUGA	X	GAA	AAUAUGUA	UACAUAUUU	GUUAGUGA
	413	GCAUCACU	CUGAUGA	X	GAA	ACAAAUAU	AUAUUUGUU	AGUGAUGC
	414	UGCAUCAC	CUGAUGA	X	GAA	AACAAAUA	UAUUUGUUA	GUGAUGCA
	429	UAUGAAAG	CUGAUGA	X	GAA	ACUCCCUG	CAGGGAGUC	CUUUCAUA

	432	CUCUAUGA	CUGAUGA	X	GAA	AGGACUCC	GGAGUCCUU	UCAUAGAG
	433	UCUCUAUG	CUGAUGA	X	GAA	AAGGACUC	GAGUCCUUU	CAUAGAGA
	434	AUCUCUAU	CUGAUGA	X	GAA	AAAGGACU	AGUCCUUUC	AUAGAGAU
	437	UGCAUCUC	CUGAUGA	X	GAA	AUGAAAGG	CCUUUCAUA	GAGAUGCA
5	455	AGUUUGGG	CUGAUGA	X	GAA	AUGUCAGU	ACUGACAUA	CCCAAACU
	464	AUGUGCAC	CUGAUGA	X	GAA	AGUUUGGG	CCCAAACUU	GUGCACAU
	491	GGGAUGAU	CUGAUGA	X	GAA	AGCUGUCU	AGACAGCUC	AUCAUCCC
	494	CAGGGGAU	CUGAUGA	X	GAA	AUGAGCUG	CAGCUCAUC	AUCCCCUG
	497	CGGCAGGG	CUGAUGA	X	GAA	AUGAUGAG	CUCAUCAUC	CCCUGCCG
10	514	CGUUGGGU	CUGAUGA	X	GAA	ACGUCACC	GGUGACGUC	ACCCAACG
	524	GUGACUGU	CUGAUGA	X	GAA	ACGUUGGG	CCCAACGUC	ACAGUCAC
	530	UUUAGGGU	CUGAUGA	X	GAA	ACUGUGAC	GUCACAGUC	ACCCUAAA
	536	AACUUUUU	CUGAUGA	X	GAA	AGGGUGAC	GUCACCCUA	AAAAAGUU
	544	CAAAUGGA	CUGAUGA	X	GAA	ACUUUUUU	AAAAAAGUU	UCCAUUUG
15	54 5	UCAAAUGG	CUGAUGA	X	GAA	AACUUUUU	AAAAAGUUU	CCAUUUGA
	54 6	AUCAAAUG	CUGAUGA	X	GAA	AAACUUUU	AAAAGUUUC	CAUUUGAU
	550	GAGUAUCA	CUGAUGA	X	GAA	AUGGAAAC	GUUUCCAUU	UGAUACUC
	551	AGAGUAUC	CUGAUGA	X	GAA	AAUGGAAA	UUUCCAUUU	GAUACUCU
	555	GGUAAGAG	CUGAUGA	X	GAA	AUCAAAUG	CAUUUGAUA	CUCUUACC
20	558	AGGGGUAA	CUGAUGA	X	GAA	AGUAUCAA	UUGAUACUC	UUACCCCU
	560	UCAGGGGU	CUGAUGA	X	GAA	AGAGUAUC	GAUACUCUU	ACCCCUGA
	561	AUCAGGGG	CUGAUGA	X	GAA	AAGAGUAU	AUACUCUUA	CCCCUGAU
	581	UCCCAUGU	CUGAUGA	X	GAA	AUUCUUUG	CAAAGAAUA	ACAUGGGA
	594	GCCUCUCC	CUGAUGA	X	GAA	ACUGUCCC	GGGACAGUA	GGAGAGGC
25	604	CUAUUAUA	CUGAUGA	X	GAA	AGCCUCUC	GAGAGGCUU	UAUAAUAG
	605	GCUAUUAU	CUGAUGA	X	GAA	AAGCCUCU	AGAGGCUUU	AUAAUAGC
	606	UGCUAUUA	CUGAUGA	X	GAA	AAAGCCUC	GAGGCUUUA	UAAUAGCA
	608	UUUGCUAU	CUGAUGA	X	GAA	AUAAAGCC	GGCUUUAUA	AUAGCAAA
	611	GCAUUUGC	CUGAUGA	X	GAA	AAAUAUUA	AUAAUAUUU	GCAAAUGC
30	625	UCUCUUUG	CUGAUGA	X	GAA	ACGUUGCA	UGCAACGUA	CAAAGAGA
	635	AGCAGUCC	CUGAUGA	X	GAA	AUCUCUUU	AAAGAGAUA	GGACUGCU
	662	UGCCCGUU	CUGAUGA	X	GAA	ACGGUGGC	GCCACCGUC	AACGGGCA
	676	UUGUCUGG	CUGAUGA	x	GAA	ACAGGUGC	GCACCUGUA	CCAGACAA

	68 8	GGGUCAGA	CUGAUGA	. x	GAA	AGUUUGUC	GACAAACUA	UCUGACCC
	69 0	AUGGGUCA	CUGAUGA	X	GAA	AUAGUUUG	CAAACUAUC	UGACCCAU
	699	GGUCUGCC	CUGAUGA	X	GAA	AUGGGUCA	UGACCCAUC	GGCAGACC
	711	UAGGAUUG	CUGAUGA	X	GAA	AUUGGUCU	AGACCAAUA	CAAUCCUA
5	716	ACAUCUAG	CUGAUGA	X	GAA	AUUGUAUU	AAUACAAUC	CUAGAUGU
	719	UGGACAUC	CUGAUGA	X	GAA	AGGAUUGU	ACAAUCCUA	GAUGUCCA
	725	CGUAUUUG	CUGAUGA	X	GAA	ACAUCUAG	CUAGAUGUC	CAAAUACG
	731	GGCGGGCG	CUGAUGA	X	GAA	AUUUGGAC	GUCCAAAUA	CGCCCGCC
	7 58	UGCCCGUG	CUGAUGA	X	GAA	AGCAGUCU	AGACUGCUC	CACGGGCA
10	771	GAGGACAA	CUGAUGA	X	GAA	AGUCUGCC	GGCAGACUC	UUGUCCUC
	77 3	UUGAGGAC	CUGAUGA	X	GAA	AGAGUCUG	CAGACUCUU	GUCCUCAA
	776	CAGUUGAG	CUGAUGA	X	GAA	ACAAGAGU	ACUCUUGUC	CUCAACUG
	77 9	GUGCAGUU	CUGAUGA	X	GAA	AGGACAAG	CUUGUCCUC	AACUGCAC
	803	CUCGUAUU	CUGAUGA	X	GAA	AGCUCCGU	ACGGAGCUC	AAUACGAG
15	807	CACCCUCG	CUGAUGA	X	GAA	AUUGAGCU	AGCUCAAUA	CGAGGGUG
	831	ACCAGGGU	CUGAUGA	X	GAA	AUUCCAGC	GCUGGAAUU	ACCCUGGU
	832	UACCAGGG	CUGAUGA	X	GAA	AAUUCCAG	CUGGAAUUA	CCCUGGUA
	840	AGUUGCUU	CUGAUGA	X	GAA	ACCAGGGU	ACCCUGGUA	AAGCAACU
	849	UGCUCUCU	CUGAUGA	X	GAA	AGUUGCUU	AAGCAACUA	AGAGAGCA
20	85 9	GCCUUAUA	CUGAUGA	X	GAA	AUGCUCUC	GAGAGCAUC	UAUAAGGC
	861	CUGCCUUA	CUGAUGA	X	GAA	AGAUGCUC	GAGCAUCUA	UAAGGCAG
	863	CGCUGCCU	CUGAUGA	X	GAA	AUAGAUGC	GCAUCUAUA	AGGCAGCG
	87 5	CUCCGGUC	CUGAUGA	X	GAA	AUCCGCUG	CAGCGGAUU	GACCGGAG
	888	GUUGUGGG	CUGAUGA	X	GAA	AUGGCUCC	GGAGCCAUU	CCCACAAC
25	889	UGUUGUGG	CUGAUGA	X	GAA	AAUGGCUC	GAGCCAUUC	CCACAACA
	904	CACUGUGG	CUGAUGA	X	GAA	ACACAUUG	CAAUGUGUU	CCACAGUG
	905	ACACUGUG	CUGAUGA	X	GAA	AACACAUU	AAUGUGUUC	CACAGUGU
	914	AUCUUAAG	CUGAUGA	X	GAA	ACACUGUG	CACAGUGUU	CUUAAGAU
	91 5	GAUCUUAA	CUGAUGA	X	GAA	AACACUGU	ACAGUGUUC	UUAAGAUC
30	917	UUGAUCUU	CUGAUGA	X	GAA	AGAACACU	AGUGUUCUU	AAGAUCAA
	918	GUUGAUCU	CUGAUGA	X	GAA	AAGAACAC	GUGUUCUUA	AGAUCAAC
	923	ACAUUGUU	CUGAUGA	X	GAA	AUCUUAAG	CUUAAGAUC	AACAAUGU
	953	CAGGUGUA	CUGAUGA	X	GAA	AGCCCCUU	AAGGGGCUC	UACACCUG

	955	GACAGGUG	CUGAUGA	X	GAA	AGAGCCCC	GGGGCUCUA	CACCUGUC
	963	CUUCACGC	CUGAUGA	X	GAA	ACAGGUGU	ACACCUGUC	GCGUGAAG
	97 9	GGAACGAG	CUGAUGA	X	GAA	ACCCACUC	GAGUGGGUC	CUCGUUCC
	982	ACUGGAAC	CUGAUGA	x	GAA	AGGACCCA	UGGGUCCUC	GUUCCAGU
5	985	AAGACUGG	CUGAUGA	X	GAA	ACGAGGAC	GUCCUCGUU	CCAGUCUU
	986	AAAGACUG	CUGAUGA	X	GAA	AACGAGGA	UCCUCGUUC	CAGUCUUU
	991	UGUUGAAA	CUGAUGA	X	GAA	ACUGGAAC	GUUCCAGUC	UUUCAACA
	993	GGUGUUGA	CUGAUGA	X	GAA	AGACUGGA	UCCAGUCUU	UCAACACC
	994	AGGUGUUG	CUGAUGA	x	GAA	AAGACUGG	CCAGUCUUU	CAACACCU
10	995	GAGGUGUU	CUGAUGA	X	GAA	AAAGACUG	CAGUCUUUC	AACACCUC
	1003	CAUGCACG	CUGAUGA	X	GAA	AGGUGUUG	CAACACCUC	CGUGCAUG
	1015	CUUUUUCA	CUGAUGA	X	GAA	ACACAUGC	GCAUGUGUA	UGAAAAAG
	1027	CACUGAUG	CUGAUGA	X	GAA	AUCCUUUU	AAAAGGAUU	CAUCAGUG
	1028	ACACUGAU	CUGAUGA	x	GAA	AAUCCUUU	AAAGGAUUC	AUCAGUGU
15	1031	UUCACACU	CUGAUGA	X	GAA	AUGAAUCC	GGAUUCAUC	AGUGUGAA
	1044	CUGCUUCC	CUGAUGA	X	GAA	AUGUUUCA	UGAAACAUC	GGAAGCAG
	1084	GCCGAUAG	CUGAUGA	X	GAA	ACCGUCUU	AAGACGGUC	CUAUCGGC
	1087	ACAGCCGA	CUGAUGA	X	GAA	AGGACCGU	ACGGUCCUA	UCGGCUGU
	1089	GGACAGCC	CUGAUGA	X	GAA	AUAGGACC	GGUCCUAUC	GGCUGUCC
20	1096	CUUUCAUG	CUGAUGA	X	GAA	ACAGCCGA	UCGGCUGUC	CAUGAAAG
	1114	GGGAGGGG	CUGAUGA	X	GAA	AGGCCUUC	GAAGGCCUU	ccccuccc
	1115	GGGGAGGG	CUGAUGA	X	GAA	AAGGCCUU	AAGGCCUUC	cccucccc
	1120	UUUCUGGG	CUGAUGA	X	GAA	AGGGGAAG	cuuccccuc	CCCAGAAA
	1130	AACCAUAC	CUGAUGA	X	GAA	AUUUCUGG	CCAGAAAUC	GUAUGGUU
25	1133	UUUAACCA	CUGAUGA	X	GAA	ACGAUUUC	GAAAUCGUA	UGGUUAAA
	1138	CAUCUUUU	CUGAUGA	X	GAA	ACCAUACG	CGUAUGGUU	AAAAGAUG
	1139	CCAUCUUU	CUGAUGA	X	GAA	AACCAUAC	GUAUGGUUA	AAAGAUGG
	1150	UUGCAGGC	CUGAUGA	X	GAA	AGCCAUCU	AGAUGGCUC	GCCUGCAA
	1162	CAGACUUC	CUGAUGA	X	GAA	AUGUUGCA	UGCAACAUU	GAAGUCUG
30	1168	AGCGAGCA	CUGAUGA	X	GAA	ACUUCAAU	AUUGAAGUC	UGCUCGCU
	1173	CAAAUAGC	CUGAUGA	X	GAA	AGCAGACU	AGUCUGCUC	GCUAUUUG
	1177	GUACCAAA	CUGAUGA	X	GAA	AGCGAGCA	UGCUCGCUA	UUUGGUAC
	1179	AUGUACCA	CUGAUGA	X	GAA	AUAGCGAG	CUCGCUAUU	UGGUACAU

	1180	CAUGUACC	CUGAUGA	X	GAA	AAUAGCGA	UCGCUAUUU	GGUACAUG
	1184	UAGCCAUG	CUGAUGA	X	GAA	ACCAAAUA	UAUUUGGUA	CAUGGCUA
	1192	UUAAUGAG	CUGAUGA	X	GAA	AGCCAUGU	ACAUGGCUA	CUCAUUAA
	1195	UAAUUAAU	CUGAUGA	X	GAA	AGUAGCCA	UGGCUACUC	AUUAAUUA
5	1198	UGAUAAUU	CUGAUGA	X	GAA	AUGAGUAG	CUACUCAUU	AAUUAUCA
	1199	UUGAUAAU	CUGAUGA	X	GAA	AAUGAGUA	UACUCAUUA	AUUAUCAA
	1202	UCUUUGAU	CUGAUGA	X	GAA	AUUAAUGA	UCAUUAAUU	AUCAAAGA
	1203	AUCUUUGA	CUGAUGA	X	GAA	AAUUAAUG	CAUUAAUUA	UCAAAGAU
	1205	ACAUCUUU	CUGAUGA	X	GAA	AAUUAAUA	UUAAUUAUC	AAAGAUGU
10	1237	AGAUCGUA	CUGAUGA	X	GAA	AGUCCCCU	AGGGGACUA	UACGAUCU
	1239	CAAGAUCG	CUGAUGA	X	GAA	AUAGUCCC	GGGACUAUA	CGAUCUUG
	1244	CCCAGCAA	CUGAUGA	X	GAA	AUCGUAUA	UAUACGAUC	UUGCUGGG
	1246	UGCCCAGC	CUGAUGA	X	GAA	AGAUCGUA	UACGAUCUU	GCUGGGCA
	1256	GACUGCUU	CUGAUGA	X	GAA	AUGCCCAG	CUGGGCAUA	AAGCAGUC
15	1264	AUAGCCUU	CUGAUGA	X	GAA	ACUGCUUU	AAAGCAGUC	AAGGCUAU
	1271	UUUUUAAA	CUGAUGA	X	GAA	AGCCUUGA	UCAAGGCUA	UUUAAAAA
	1273	GGUUUUUA	CUGAUGA	X	GAA	AUAGCCUU	AAGGCUAUU	UAAAAACC
	1274	AGGUUUUU	CUGAUGA	X	GAA	AAUAGCCU	AGGCUAUUU	AAAAACCU
	1275	GAGGUUUU	CUGAUGA	X	GAA	AAAUAGCC	GGCUAUUUA	AAAACCUC
20	1283	GUGGCAGU	CUGAUGA	X	GAA	AGGUUUUU	AAAAACCUC	ACUGCCAC
	1293	UACAAUGA	CUGAUGA	X	GAA	AGUGGCAG	CUGCCACUC	UCAUUGUA
	1295	UUUACAAU	CUGAUGA	X	GAA	AGAGUGGC	GCCACUCUC	AUUGUAAA
	1298	ACGUUUAC	CUGAUGA	X	GAA	AUGAGAGU	ACUCUCAUU	GUAAACGU
	1301	UUCACGUU	CUGAUGA	X	GAA	ACAAUGAG	CUCAUUGUA	AACGUGAA
25	1314	GUAGAUCU	CUGAUGA	X	GAA	AGGUUUCA	UGAAACCUC	AGAUCUAC
	1319	UUUUCGUA	CUGAUGA	X	GAA	AUCUGAGG	CCUCAGAUC	UACGAAAA
	1321	ACUUUUCG	CUGAUGA	X	GAA	AGAUCUGA	UCAGAUCUA	CGAAAAGU
	1330	AGGACACG	CUGAUGA	Х	GAA	ACUUUUCG	CGAAAAGUC	CGUGUCCU
	1336	GAAGCGAG	CUGAUGA	X	GAA	ACACGGAC	GUCCGUGUC	CUCGCUUC
30	1339	UUGGAAGC	CUGAUGA	X	GAA	AGGACACG	CGUGUCCUC	GCUUCCAA
	1343	GGGCUUGG	CUGAUGA	X	GAA	AGCGAGGA	UCCUCGCUU	CCAAGCCC
	1344					AAGCGAGG	CCUCGCUUC	CAAGCCCA
	1356	CGGAUAGA	CUGAUGA	X	GAA	AGGUGGGC	GCCCACCUC	UCUAUCCG

PCT/US96/17480

WO 97/15662

	1358	AGCGGAUA	CUGAUGA	x	GAA	AGAGGUGG	CCACCUCUC	UAUCCGCU
	1360	CCAGCGGA	CUGAUGA	X	GAA	AGAGAGGU	ACCUCUCUA	UCCGCUGG
	1362	GCCCAGCG	CUGAUGA	x	GAA	AUAGAGAG	CUCUCUAUC	CGCUGGGC
	1382	CAAGUGAG	CUGAUGA	X	GAA	ACUUGUCU	AGACAAGUC	CUCACUUG
5	1385	GUGCAAGU	CUGAUGA	x	GAA	AGGACUUG	CAAGUCCUC	ACUUGCAC
	1389	CACGGUGC	CUGAUGA	x	GAA	AGUGAGGA	UCCUCACUU	GCACCGUG
	1399	GGAUGCCA	CUGAUGA	X	GAA	ACACGGUG	CACCGUGUA	UGGCAUCC
	1406	GGCCGAGG	CUGAUGA	X	GAA	AUGCCAUA	UAUGGCAUC	CCUCGGCC
	1410	UGUUGGCC	CUGAUGA	X	GAA	AGGGAUGC	GCAUCCCUC	GGCCAACA
10	1421	AGCCACGU	CUGAUGA	X	GAA	AUUGUUGG	CCAACAAUC	ACGUGGCU
	1430	GGGUGCCA	CUGAUGA	X	GAA	AGCCACGU	ACGUGGCUC	UGGCACCC
	1443	AUUGUGGU	CUGAUGA	X	GAA	ACAGGGGU	ACCCCUGUC	ACCACAAU
	1452	UUUGGAGU	CUGAUGA	X	GAA	AUUGUGGU	ACCACAAUC	ACUCCAAA
	1456	UUUCUUUG	CUGAUGA	X	GAA	AGUGAUUG	CAAUCACUC	CAAAGAAA
15	1468	AGAAGUCA	CUGAUGA	X	GAA	ACCUUUCU	AGAAAGGUA	UGACUUCU
	1474	CAGUGCAG	CUGAUGA	X	GAA	AGUCAUAC	GUAUGACUU	CUGCACUG
	1475	UCAGUGCA	CUGAUGA	X	GAA	AAGUCAUA	UAUGACUUC	UGCACUGA
	1495	GGAUAAAG	CUGAUGA	X	GAA	AUUCUUCA	UGAAGAAUC	CUUUAUCC
	1498	CCAGGAUA	CUGAUGA	X	GAA	AGGAUUCU	AGAAUCCUU	UAUCCUGG
20	1499	UCCAGGAU	CUGAUGA	X	GAA	AAGGAUUC	GAAUCCUUU	AUCCUGGA
	1500	AUCCAGGA	CUGAUGA	X	GAA	AAAGGAUU	AAUCCUUUA	UCCUGGAU
	1502	GGAUCCAG	CUGAUGA	X	GAA	AUAAAGGA	UCCUUUAUC	CUGGAUCC
	1509	GCUGCUGG	CUGAUGA	X	GAA	AUCCAGGA	UCCUGGAUC	CCAGCAGC
	1522	UGUUUCCU	CUGAUGA	X	GAA	AGUUGCUG	CAGCAACUU	AGGAAACA
25	1523	CUGUUUCC	CUGAUGA	X	GAA	AAGUUGCU	AGCAACUUA	GGAAACAG
	1535	AUGCUCUC	CUGAUGA	X	GAA	AUUCUGUU	AACAGAAUU	GAGAGCAU
	1544	CGCUGAGA	CUGAUGA	X	GAA	AUGCUCUC	GAGAGCAUC	UCUCAGCG
	1546	UGCGCUGA	CUGAUGA	X	GAA	AGAUGCUC	GAGCAUCUC	UCAGCGCA
	1548	CAUGCGCU	CUGAUGA	X	GAA	AGAGAUGC	GCAUCUCUC	AGCGCAUG
30	1562	CCUUCUAU	CUGAUGA	X	GAA	ACCGUCAU	AUGACGGUC	AUAGAAGG
	1565	GUUCCUUC	CUGAUGA	X	GAA	AUGACCGU	ACGGUCAUA	GAAGGAAC
	1578	AACCGUCU	CUGAUGA	X	GAA	AUUUGUUC	GAACAAAUA	AGACGGUU
	1586	AAUGUGCU	CUGAUGA	X	GAA	ACCGUCUU	AAGACGGUU	AGCACAUU

	1587	CAAUGUGC	CUGAUGA	X	GAA	AACCGUCU	AGACGGUUA	GCACAUUG
	1594	CCACCACC	CUGAUGA	X	GAA	AUGUGCUA	UAGCACAUU	GGUGGUGG
	1609	GGGUCUGA	CUGAUGA	X	GAA	AGUCAGCC	GGCUGACUC	UCAGACCC
	1611	AGGGGUCU	CUGAUGA	X	GAA	AGAGUCAG	CUGACUCUC	AGACCCCU
5	1625	CAGCUGUA	CUGAUGA	X	GAA	AUUCCAGG	CCUGGAAUC	UACAGCUG
	1627	GGCAGCUG	CUGAUGA	X	GAA	AGAUUCCA	UGGAAUCUA	CAGCUGCC
	1642	UUUUAUUG	CUGAUGA	X	GAA	AGGCCCGG	CCGGGCCUU	CAAUAAAA
	1643	AUUUUAUU	CUGAUGA	X	GAA	AAGGCCCG	CGGGCCUUC	AAUAAAU
	1647	CCCUAUUU	CUGAUGA	X	GAA	AUUGAAGG	CCUUCAAUA	AAAUAGGG
10	1652	ACAGUCCC	CUGAUGA	X	GAA	UUAUUUA	AAUAAAAUA	GGGACUGU
	1673	UUUAAAAUUU	CUGAUGA	X	GAA	AUGUUUCU	AGAAACAUA	AAAUUUUA
	1678	UGACAUAA	CUGAUGA	X	GAA	AUUUUAUG	CAUAAAAUU	UUAUGUCA
	1679	GUGACAUA	CUGAUGA	X	GAA	UAUUUUAA	AUAAAAUUU	UAUGUCAC
	1680	UGUGACAU	CUGAUGA	X	GAA	AUUUUAAA	UUUUAAAAUUUU	AUGUCACA
15	1681	CUGUGACA	CUGAUGA	X	GAA	UUUUAAAA	AAAAUUUUA	UGUCACAG
	1685	ACAUCUGU	CUGAUGA	X	GAA	ACAUAAAA	UUUUAUGUC	ACAGAUGU
	1705	AAACGUGA	CUGAUGA	X	GAA	AGCCAUUC	GAAUGGCUU	UCACGUUU
	1706	GAAACGUG	CUGAUGA	X	GAA	AAGCCAUU	AAUGGCUUU	CACGUUUC
	1707	GGAAACGU	CUGAUGA	X	GAA	AAAGCCAU	AUGGCUUUC	ACGUUUCC
20	1712	UCCAAGGA	CUGAUGA	X	GAA	ACGUGAAA	UUUCACGUU	UCCUUGGA
	1713	UUCCAAGG	CUGAUGA	X	GAA	AACGUGAA	UUCACGUUU	CCUUGGAA
	1714	UUUCCAAG	CUGAUGA	X	GAA	AAACGUGA	UCACGUUUC	CUUGGAAA
	1717	ncnnnncc	CUGAUGA	X	GAA	AGGAAACG	CGUUUCCUU	GGAAAAGA
	1756	CCACACAG	CUGAUGA	X	GAA	ACAGUUUC	GAAACUGUC	CUGUGUGG
25	1766	UUAUUUAA	CUGAUGA	X	GAA	ACCACACA	UGUGUGGUC	UUAAAUUA
	1770	CAGGAAUU	CUGAUGA	X	GAA	AUUGACCA	UGGUCAAUA	AAUUCCUG
	1774	UGUACAGG	CUGAUGA	X	GAA	AUUUAUUG	CAAUAAAUU	CCUGUACA
	1775	CUGUACAG	CUGAUGA	X	GAA	UUAUUUAA	AAUAAAUUC	CUGUACAG
	1780	UGUCUCUG	CUGAUGA	X	GAA	ACAGGAAU	AUUCCUGUA	CAGAGACA
30	1790	AUCCAGGU	CUGAUGA	X	GAA	AUGUCUCU	AGAGACAUU	ACCUGGAU
	1791					AAUGUCUC	GAGACAUUA	CCUGGAUU
	1799					AUCCAGGU	ACCUGGAUU	CUGCUACG
	1800	CCGUAGCA	CUGAUGA	X	GAA	AAUCCAGG	CCUGGAUUC	UGCUACGG

	1805	ACUGUCCG	CUGAUGA	X	GAA	AGCAGAAU	AUUCUGCUA	CGGACAGU
	1814	CUGUUGUU	CUGAUGA	X	GAA	ACUGUCCG	CGGACAGUU	AACAACAG
	1815	ucuguugu	CUGAUGA	X	GAA	AACUGUCC	GGACAGUUA	ACAACAGA
	1836	GCUGAUAC	CUGAUGA	X	GAA	AUGGUGCA	UGCACCAUA	GUAUCAGC
5	1839	CUUGCUGA	CUGAUGA	X	GAA	ACUAUGGU	ACCAUAGUA	UCAGCAAG
	1841	UGCUUGCU	CUGAUGA	X	GAA	AUACUAUG	CAUAGUAUC	AGCAAGCA
	1866	GUAAUCUU	CUGAUGA	X	GAA	AGUGGUGG	CCACCACUC	AAGAUUAC
	1872	GAUGGAGU	CUGAUGA	X	GAA	AUCUUGAG	CUCAAGAUU	ACUCCAUC
	1873	UGAUGGAG	CUGAUGA	X	GAA	AAUCUUGA	UCAAGAUUA	CUCCAUCA
10	1876	GAGUGAUG	CUGAUGA	X	GAA	AGUAAUCU	AGAUUACUC	CAUCACUC
	1880	UUCAGAGU	CUGAUGA	X	GAA	AUGGAGUA	UACUCCAUC	ACUCUGAA
	1884	AAGGUUCA	CUGAUGA	X	GAA	AGUGAUGG	CCAUCACUC	UGAACCUU
	1892	UUGAUGAC	CUGAUGA	X	GAA	AGGUUCAG	CUGAACCUU	GUCAUCAA
	1895	UUCUUGAU	CUGAUGA	X	GAA	ACAAGGUU	AACCUUGUC	AUCAAGAA
15	1898	ACGUUCUU	CUGAUGA	X	GAA	AUGACAAG	CUUGUCAUC	AAGAACGU
	1909	CUUCUAGA	CUGAUGA	X	GAA	ACACGUUC	GAACGUGUC	UCUAGAAG
	1911	GUCUUCUA	CUGAUGA	X	GAA	AGACACGU	ACGUGUCUC	UAGAAGAC
	1 91 3	GAGUCUUC	CUGAUGA	X	GAA	AGAGACAC	GUGUCUCUA	GAAGACUC
	1921	AGGUGCCC	CUGAUGA	X	GAA	AGUCUUCU	AGAAGACUC	GGGCACCU
20	1930	UGCACGCA	CUGAUGA	X	GAA	AGGUGCCC	GGGCACCUA	UGCGUGCA
	1952	CCUGUGUA	CUGAUGA	X	GAA	AUGUUCCU	AGGAACAUA	UACACAGG
	1954	CCCCUGUG	CUGAUGA	X	GAA	AUAUGUUC	GAACAUAUA	CACAGGGG
	1970	UUCCGAAG	CUGAUGA	x	GAA	AUGUCUUC	GAAGACAUC	CUUCGGAA
	1973	GUCUUCCG	CUGAUGA	X	GAA	AGGAUGUC	GACAUCCUU	CGGAAGAC
25	1974	UGUCUUCC	CUGAUGA	X	GAA	AAGGAUGU	ACAUCCUUC	GGAAGACA
	1988	CUAACGAG	CUGAUGA	X	GAA	ACUUCUGU	ACAGAAGUU	CUCGUUAG
	1 98 9	UCUAACGA	CUGAUGA	X	GAA	AACUUCUG	CAGAAGUUC	UCGUUAGA
	1991	UCUCUAAC	CUGAUGA	X	GAA	AGAACUUC	GAAGUUCUC	GUUAGAGA
	1994	GAAUCUCU	CUGAUGA	X	GAA	ACGAGAAC	GUUCUCGUU	AGAGAUUC
30	1995	CGAAUCUC	CUGAUGA	X	GAA	AACGAGAA	UUCUCGUUA	GAGAUUCG
	2001	CGCUUCCG	CUGAUGA	X	GAA	AUCUCUAA	UUAGAGAUU	CGGAAGCG
	2002	GCGCUUCC	CUGAUGA	X	GAA	AAUCUCUA	UAGAGAUUC	GGAAGCGC
	2021	AGGUUUUG	CUGAUGA	X	GAA	AGCAGGUG	CACCUGCUU	CAAAACCU

	2022	GAGGUUUU	CUGAUGA	X	GAA	AAGCAGGU	ACCUGCUUC	AAAACCUC
	2030	UAGUCACU	CUGAUGA	X	GAA	AGGUUUUG	CAAAACCUC	AGUGACUA
	2038	AGACCUCG	CUGAUGA	X	GAA	AGUCACUG	CAGUGACUA	CGAGGUCU
	2045	CUGAUGGA	CUGAUGA	X	GAA	ACCUCGUA	UACGAGGUC	UCCAUCAG
5	2047	CACUGAUG	CUGAUGA	X	GAA	AGACCUCG	CGAGGUCUC	CAUCAGUG
	2051	GAGCCACU	CUGAUGA	X	GAA	AUGGAGAC	GUCUCCAUC	AGUGGCUC
	2059	AGGUCGUA	CUGAUGA	X	GAA	AGCCACUG	CAGUGGCUC	UACGACCU
	2061	UAAGGUCG	CUGAUGA	X	GAA	AGAGCCAC	GUGGCUCUA	CGACCUUA
	2068	GACAGUCU	CUGAUGA	X	GAA	AGGUCGUA	UACGACCUU	AGACUGUC
10	2069	UGACAGUC	CUGAUGA	X	GAA	AAGGUCGU:	ACGACCUUA	GACUGUCA
	2076	UCUAGCUU	CUGAUGA	X	GAA	ACAGUCUA	UAGACUGUC	AAGCUAGA
	2082	GACACCUC	CUGAUGA	X	GAA	AGCUUGAC	GUCAAGCUA	GAGGUGUC
	2090	GGCGCGGG	CUGAUGA	X	GAA	ACACCUCU	AGAGGUGUC	CCCGCGCC
	2100	AGUGAUCU	CUGAUGA	X	GAA	AGGCGCGG	CCGCGCCUC	AGAUCACU
15	2105	AACCAAGU	CUGAUGA	X	GAA	AUCUGAGG	CCUCAGAUC	ACUUGGUU
	2109	UUUGAACC	CUGAUGA	X	GAA	AGUGAUCU	AGAUCACUU	GGUUCAAA
	2113	UGUUUUUG	CUGAUGA	X	GAA	ACCAAGUG	CACUUGGUU	CAAAAACA
	2114	UUGUUUUU	CUGAUGA	X	GAA	AACCAAGU	ACUUGGUUC	AAAAACAA
	2132	UCUUGUUG	CUGAUGA	X	GAA	AUUUUGUG	CACAAAAUA	CAACAAGA
20	2150	CCUAAAAU	CUGAUGA	X	GAA	AUUCCCGG	CCGGGAAUU	AUUUUAGG
	2151	UCCUAAAA	CUGAUGA	X	GAA	AAUUCCCG	CGGGAAUUA	UUUUAGGA
	215 3	GGUCCUAA	CUGAUGA	X	GAA	AUAAUUCC	GGAAUUAUU	UUAGGACC
	2154	UGGUCCUA	CUGAUGA	X	GAA	AAUAAUUC	GAAUUAUUU	UAGGACCA
	2155	CUGGUCCU	CUGAUGA	X	GAA	UUAAUAAA	UUUUUAUUUAA	AGGACCAG
25	2156	CCUGGUCC	CUGAUGA	X	GAA	UAAUAAA	AUUUUUUA	GGACCAGG
	2179	UUUCAAUA	CUGAUGA	X	GAA	ACAGCGUG	CACGCUGUU	UAUUGAAA
	2180	CUUUCAAU	CUGAUGA	X	GAA	AACAGCGU	ACGCUGUUU	AUUGAAAG
	2181	UCUUUCAA	CUGAUGA	X	GAA	AAACAGCG	CGCUGUUUA	UUGAAAGA
	2183	ACUCUUUC	CUGAUGA	X	GAA	AUAAACAG	CUGUUUAUU	GAAAGAGU
30	2192	UCCUCUGU	CUGAUGA	X	GAA	ACUCUUUC	GAAAGAGUC	ACAGAGGA
	2213	CACCUAUA					GAGGGUGUC	UAUAGGUG
	2215	GGCACCUA					GGGUGUCUA	UAGGUGCC
	2217	UCGGCACC	CUGAUGA	X	GAA	AUAGACAC	GUGUCUAUA	GGUGCCGA

	2263	CGGUGAGG	CUGAUGA	X	GAA	AGGCUGCG	CGCAGCCUA	CCUCACCG
	2267	UGCACGGU	CUGAUGA	X	GAA	AGGUAGGC	GCCUACCUC	ACCGUGCA
	2284	ACUUGUCU	CUGAUGA	X	GAA	AGGUUCCU	AGGAACCUC	AGACAAGU
	2293	CCAGGUUU	CUGAUGA	X	GAA	ACUUGUCU	AGACAAGUC	AAACCUGG
5	2309	GUGAGCGU	CUGAUGA	x	GAA	AUCAGCUC	GAGCUGAUC	ACGCUCAC
	2315	GUGCACGU	CUGAUGA	x	GAA	AGCGUGAU	AUCACGCUC	ACGUGCAC
	2342	AGCCAAAA	CUGAUGA	X	GAA	AGGGUCGC	GCGACCCUC	UUUUGGCU
	2344	GGAGCCAA	CUGAUGA	X	GAA	AGAGGGUC	GACCCUCUU	UUGGCUCC
	2345	AGGAGCCA	CUGAUGA	X	GAA	AAGAGGGU	ACCCUCUUU	UGGCUCCU
10	2346	AAGGAGCC	CUGAUGA	X	GAA	AAAGAGGG	cccucuuuu	GGCUCCUU
	2351	GUUAGAAG	CUGAUGA	X	GAA	AGCCAAAA	UUUUGGCUC	CUUCUAAC
	2354	AGAGUUAG	CUGAUGA	X	GAA	AGGAGCCA	UGGCUCCUU	CUAACUCU
	2355	GAGAGUUA	CUGAUGA	X	GAA	AAGGAGCC	GGCUCCUUC	UAACUCUC
	2357	AAGAGAGU	CUGAUGA	X	GAA	AGAAGGAG	CUCCUUCUA	ACUCUCUU
15	2361	GAUGAAGA	CUGAUGA	X	GAA	AGUUAGAA	UUCUAACUC	UCUUCAUC
	2363	CUGAUGAA	CUGAUGA	X	GAA	AGAGUUAG	CUAACUCUC	UUCAUCAG
	2365	UUCUGAUG	CUGAUGA	X	GAA	AGAGAGUU	AACUCUCUU	CAUCAGAA
	2366	UUUCUGAU	CUGAUGA	X	GAA	AAGAGAGU	ACUCUCUUC	AUCAGAAA
	2369	AGUUUUCU	CUGAUGA	X	GAA	AUGAAGAG	CUCUUCAUC	AGAAAACU
20	2386	CGGAAGAA	CUGAUGA	X	GAA	ACCGCUUC	GAAGCGGUC	UUCUUCCG
	2388	UUCGGAAG	CUGAUGA	X	GAA	AGACCGCU	AGCGGUCUU	CUUCCGAA
	2389	CUUCGGAA	CUGAUGA	X	GAA	AAGACCGC	GCGGUCUUC	UUCCGAAG
	2391	UACUUCGG	CUGAUGA	X	GAA	AGAAGACC	GGUCUUCUU	CCGAAGUA
	2392	UUACUUCG	CUGAUGA	X	GAA	AAGAAGAC	GUCUUCUUC	CGAAGUAA
25	2399	UCUGUCUU	CUGAUGA	X	GAA	ACUUCGGA	UCCGAAGUA	AAGACAGA
	2410	UUGACAGG	CUGAUGA	X	GAA	AGUCUGUC	GACAGACUA	CCUGUCAA
	2416	UAAUGAUU	CUGAUGA	X	GAA	ACAGGUAG	CUACCUGUC	AAUCAUUA
	2420	UCCAUAAU	CUGAUGA	X	GAA	AUUGACAG	CUGUCAAUC	AUUAUGGA
	2423	GGGUCCAU	CUGAUGA	X	GAA	AUGAUUGA	UCAAUCAUU	AUGGACCC
30	2424	UGGGUCCA	CUGAUGA	X	GAA	AAUGAUUG	CAAUCAUUA	UGGACCCA
	2441	UCCAGGGG	CUGAUGA	X	GAA	ACUUCAUC	GAUGAAGUU	CCCCUGGA
	2442	AUCCAGGG	CUGAUGA	X	GAA	AACUUCAU	AUGAAGUUC	CCCUGGAU
	2473	UGGCAUCA	CUGAUGA	X	GAA	AGGGCAGC	GCUGCCCUA	UGAUGCCA

	2494	CCCGUGCA	CUGAUGA	X	GAA	ACUCCCAC	GUGGGAGUU UGCACGGG
	2495	UCCCGUGC	CUGAUGA	X	GAA	AACUCCCA	UGGGAGUUU GCACGGGA
	2516	GAUUUGCC	CUGAUGA	X	GAA	AGUUUCAG	CUGAAACUA GGCAAAUC
	2524	UUCCGAGC	CUGAUGA	X	GAA	AUUUGCCU	AGGCAAAUC GCUCGGAA
5	2528	CCUCUUCC	CUGAUGA	X	GAA	AGCGAUUU	AAAUCGCUC GGAAGAGG
	2541	UUUCCCAA	CUGAUGA	X	GAA	AGCCCCUC	GAGGGGCUU UUGGGAAA
	2542	CUUUCCCA	CUGAUGA	Х	GAA	AAGCCCCU	AGGGGCUUU UGGGAAAG
	2543	ACUUUCCC	CUGAUGA	X	GAA	AAAGCCCC	GGGGCUUUU GGGAAAGU
	2552	GCUUGAAC	CUGAUGA	X	GAA	ACUUUCCC	GGGAAAGUC GUUCAAGC
10	2555	GAGGCUUG	CUGAUGA	X	GAA	ACGACUUU	AAAGUCGUU CAAGCCUC
	2556	AGAGGCUU	CUGAUGA	X	GAA	AACGACUU	AAGUCGUUC AAGCCUCU
	2563	CAAAUGCA	CUGAUGA	X	GAA	AGGCUUGA	UCAAGCCUC UGCAUUUG
	2569	UAAUGCCA	CUGAUGA	x	GAA	AUGCAGAG	CUCUGCAUU UGGCAUUA
	2570	UUAAUGCC	CUGAUGA	X	GAA	AAUGCAGA	UCUGCAUUU GGCAUUAA
15	2576	GAUUUCUU	CUGAUGA	X	GAA	AUGCCAAA	UUUGGCAUU AAGAAAUC
	2577	UGAUUUCU	CUGAUGA	x	GAA	AAUGCCAA	UUGGCAUUA AGAAAUCA
	2584	AGGUGGGU	CUGAUGA	X	GAA	AUUUCUUA	UAAGAAAUC ACCCACCU
	2617	ccucuuuc	CUGAUGA	x	GAA	ACAUCUUC	GAAGAUGUU GAAAGAGG
	2644	GAGCUUUG	CUGAUGA	x	GAA	ACUCACUG	CAGUGAGUA CAAAGCUC
20	2652	GGUCAUCA	CUGAUGA	X	GAA	AGCUUUGU	ACAAAGCUC UGAUGACC
	2666	AAGAUCUU	CUGAUGA	X	GAA	AGUUCGGU	ACCGAACUC AAGAUCUU
	2672	UGGGUCAA	CUGAUGA	X	GAA	AUCUUGAG	CUCAAGAUC UUGACCCA
	2674	UGUGGGUC	CUGAUGA	X	GAA	AGAUCUUG	CAAGAUCUU GACCCACA
	2684	UGAUGGCC	CUGAUGA	X	GAA	AUGUGGGU	ACCCACAUC GGCCAUCA
25	2691	AUUCAGAU	CUGAUGA	X	GAA	AUGGCCGA	UCGGCCAUC AUCUGAAU
	2694	CACAUUCA	CUGAUGA	X	GAA	AUGAUGGC	GCCAUCAUC UGAAUGUG
	2705	AGGAGGUU	CUGAUGA	X	GAA	ACCACAUU	AAUGUGGUU AACCUCCU
	2706	CAGGAGGU	CUGAUGA	X	GAA	AACCACAU	AUGUGGUUA ACCUCCUG
	2711	GCUCCCAG	CUGAUGA	X	GAA	AGGUUAAC	GUUAACCUC CUGGGAGC
30	2742	CACCAUCA	CUGAUGA	X	GAA	AGGCCCUC	GAGGGCCUC UGAUGGUG
	275 3						AUGGUGAUC GUGGAAUA
	2761						CGUGGAAUA CUGCAAAU
	2770						CUGCAAAUA CGGAAACC

	2782	GGUAGUUG	CUGAUGA	X	GAA	ACAGGUUU	AAACCUGUC	CAACUACC
	2788	UCUUGAGG	CUGAUGA	X	GAA	AGUUGGAC	GUCCAACUA	CCUCAAGA
	2792	UUGCUCUU	CUGAUGA	X	GAA	AGGUAGUU	AACUACCUC	AAGAGCAA
	2809	GACAGAAU	CUGAUGA	X	GAA	AGUCACGU	ACGUGACUU	AUUCUGUC
5	2810	AGACAGAA	CUGAUGA	X	GAA	AAGUCACG	CGUGACUUA	UUCUGUCU
	2812	UGAGACAG	CUGAUGA	X	GAA	AUAAGUCA	UGACUUAUU	CUGUCUCA
	2813	UUGAGACA	CUGAUGA	X	GAA	AAUAAGUC	GACUUAUUC	UGUCUCAA
	2817	CUUGUUGA	CUGAUGA	X	GAA	ACAGAAUA	UAUUCUGUC	UCAACAAG
	2819	UCCUUGUU	CUGAUGA	X	GAA	AGACAGAA	UUCUGUCUC	AACAAGGA
10	2836	CCAUAUGC	CUGAUGA	X	GAA	AGGCUGCG	CGCAGCCUU	GCAUAUGG
	2841	GAGCUCCA	CUGAUGA	X	GAA	AUGCAAGG	CCUUGCAUA	UGGAGCUC
	2849	ucuuucuu	CUGAUGA	X	GAA	AGCUCCAU	AUGGAGCUC	AAGAAAGA
	2900	ACACUGUC	CUGAUGA	X	GAA	AGGCGGGG	CCCCGCCUA	GACAGUGU
	2909	GAGCUGCU	CUGAUGA	X	GAA	ACACUGUC	GACAGUGUC	AGCAGCUC
15	2917	UGACACUU	CUGAUGA	X	GAA	AGCUGCUG	CAGCAGCUC	AAGUGUCA
	2924	GAGCUGGU	CUGAUGA	X	GAA	ACACUUGA	UCAAGUGUC	ACCAGCUC
	2932	GGAAGCUG	CUGAUGA	X	GAA	AGCUGGUG	CACCAGCUC	CAGCUUCC
	2938	CUUCAGGG	CUGAUGA	X	GAA	AGCUGGAG	CUCCAGCUU	CCCUGAAG
	29 39	UCUUCAGG	CUGAUGA	X	GAA	AAGCUGGA	UCCAGCUUC	CCUGAAGA
20	2982	CUCACUGU	CUGAUGA	X	GAA	AUCCUCGU	ACGAGGAUU	ACAGUGAG
	2983	UCUCACUG	CUGAUGA	X	GAA	AAUCCUCG	CGAGGAUUA	CAGUGAGA
	29 93	UGCUUGGA	CUGAUGA	X	GAA	AUCUCACU	AGUGAGAUC	UCCAAGCA
	2995	GCUGCUUG	CUGAUGA	X	GAA	AGAUCUCA	UGAGAUCUC	CAAGCAGC
	3008	UCCAUGGU	CUGAUGA	X	GAA	AGGGGCUG	CAGCCCCUC	ACCAUGGA
25	3026	CUGUAGGA	CUGAUGA	X	GAA	AUCAGGUC	GACCUGAUU	UCCUACAG
	3027	ACUGUAGG	CUGAUGA	X	GAA	AAUCAGGU	ACCUGAUUU	CCUACAGU
	3028	AACUGUAG	CUGAUGA	X	GAA	AAAUCAGG	CCUGAUUUC	CUACAGUU
	3031	GGAAACUG	CUGAUGA	X	GAA	AGGAAAUC	GAUUUCCUA	CAGUUUCC
	3036	CACUUGGA	CUGAUGA	X	GAA	ACUGUAGG	CCUACAGUU	UCCAAGUG
30	3037	CCACUUGG	CUGAUGA	X	GAA	AACUGUAG	CUACAGUUU	CCAAGUGG
	3038	GCCACUUG	CUGAUGA	X	GAA	AAACUGUA	UACAGUUUC	CAAGUGGC
	3061	AGGACAGA	CUGAUGA	X	GAA	ACUCCAUG	CAUGGAGUU	UCUGUCCU
	3062	GAGGACAG	CUGAUGA	X	GAA	AACUCCAU	AUGGAGUUU	CUGUCCUC

3209 UUUAGGG CUG 3210 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG	SAUGA X GA	AAACUCCA	UGGAGUUUC	UGUCCUCC
3083 UCCCGAUG CUG 3084 GUCCCGAU CUG 3087 CAGGUCCC CUG 3110 GAUAAAAG CUG 3113 UCAGAUAA CUG 3114 CUCAGAUA CUG 3116 UUCUCAGA CUG 3140 AAGUCGCA CUG 3141 AAAGUCGC CUG 3149 GCCAGGCC CUG 3165 CUUAUAAA CUG 3167 UUCUUAUA CUG 3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3184 CCUCACAU CUG 3184 UCCUCACA CUG 3184 UCCUCACA CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3210 UUUUAGGG CUG 3210 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG	GAUGA X GA	A ACAGAAAC	GUUUCUGUC	CUCCAGAA
5 3084 GUCCCGAU CUG 3087 CAGGUCCC CUG 3110 GAUAAAAG CUG 3113 UCAGAUAA CUG 3114 CUCAGAUA CUG 3116 UUCUCAGAU CUG 3118 UGUUCUCA CUG 3140 AAGUCGCA CUG 3141 AAAGUCGC CUG 3149 GCCAGGCC CUG 3165 CUUAUAAA CUG 3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3201 AAGUCGAG CUG 3201 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG 3228 GGAUUCAG CUG 3228 GGAUUCAG CUG	SAUGA X GA	AA AGGACAGA	ucuguccuc	CAGAAAGU
3087 CAGGUCCC CUG 3110 GAUAAAAG CUG 3113 UCAGAUAA CUG 3114 CUCAGAUA CUG 3115 UCUCAGAU CUG 3116 UUCUCAGA CUG 3118 UGUUCUCA CUG 3140 AAGUCGCA CUG 3149 GCCAGGCC CUG 3149 GCCAGGCC CUG 3165 CUUAUAAA CUG 3165 CUUAUAUA CUG 3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3201 AAGUCGAG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG 3228 GGAUUCAG CUG 3228 GGAUUCAG CUG	auga x ga	A AUGCACUU	AAGUGCAUU	CAUCGGGA
3110 GAUAAAAG CUG 3113 UCAGAUAA CUG 3114 CUCAGAUA CUG 3116 UUCUCAGAU CUG 3118 UGUUCUCA CUG 3140 AAGUCGCA CUG 3141 AAAGUCGC CUG 3149 GCCAGGCC CUG 3165 CUUAUAAA CUG 3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3184 UCCUCACA CUG 3194 GGGAAGUC CUG 3201 AAGUCGAG CUG 3201 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG 3228 GGAUUCAG CUG	GAUGA X GA	A AAUGCACU	AGUGCAUUC	AUCGGGAC
3113 UCAGAUAA CUG 3114 CUCAGAUA CUG 3115 UCUCAGAU CUG 3116 UUCUCAGA CUG 3118 UGUUCUCA CUG 3140 AAGUCGCA CUG 3141 AAAGUCGC CUG 3149 GCCAGGCC CUG 3165 CUUAUAAA CUG 3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3201 AAGUCGAG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG 3228 GGAUUCAG CUG	GAUGA X GA	A AUGAAUGC	GCAUUCAUC	GGGACCUG
3114 CUCAGAUA CUG 3115 UCUCAGAU CUG 3116 UUCUCAGA CUG 3118 UGUUCUCA CUG 3140 AAGUCGCA CUG 3141 AAAGUCGC CUG 3149 GCCAGGCC CUG 3165 CUUAUAAA CUG 3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3201 AAGUCGAG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG 3228 GGAUUCAG CUG 3228 GGAUUCAG CUG	AUGA X GA	A AUGUUUCU	AGAAACAUC	CUUUUAUC
10 3115 UCUCAGAU CUG 3116 UUCUCAGA CUG 3118 UGUUCUCA CUG 3140 AAGUCGCA CUG 3141 AAAGUCGC CUG 3149 GCCAGGCC CUG 3165 CUUAUAAA CUG 3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3201 AAGUCGAG CUG 3210 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG	auga x ga	A AGGAUGUU	AACAUCCUU	UUAUCUGA
3116 UUCUCAGA CUG 3118 UGUUCUCA CUG 3140 AAGUCGCA CUG 3141 AAAGUCGC CUG 3149 GCCAGGCC CUG 3165 CUUAUAAA CUG 3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3209 UUUAGGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG 3228 GGAUUCAG CUG	AUGA X GA	A AAGGAUGU	ACAUCCUUU	UAUCUGAG
3118 UGUUCUCA CUG 3140 AAGUCGCA CUG 3141 AAAGUCGC CUG 3149 GCCAGGCC CUG 3165 CUUAUAAA CUG 3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3209 UUUAGGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG 3228 GGAUUCAG CUG	AUGA X GA	A AAAGGAUG	CAUCCUUUU	AUCUGAGA
3140 AAGUCGCA CUG 3141 AAAGUCGC CUG 3148 CCAGGCCA CUG 3149 GCCAGGCC CUG 3165 CUUAUAAA CUG 3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3209 UUUAGGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG 3228 GGAUUCAG CUG	BAUGA X GA	A AAAAGGAU	AUCCUUUUA	UCUGAGAA
3141 AAAGUCGC CUG 3149 GCCAGGCC CUG 3149 GCCAGGCC CUG 3165 CUUAUAAA CUG 3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3201 GGGAAGUC CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG 3228 GGAUUCAG CUG	auga x ga	A AUAAAAGG	CCUUUUAUC	UGAGAACA
15 3148 CCAGGCCA CUG 3149 GCCAGGCC CUG 3165 CUUAUAAA CUG 3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3169 GGUUCUUA CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3201 GGGAAGUC CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG 3228 GGAUUCAG CUG	AUGA X GA	A AUCUUCAC	GUGAAGAUU	UGCGACUU
3149 GCCAGGCC CUG 3165 CUUAUAAA CUG 3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3169 GGUUCUUA CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3209 UUUAGGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG	AUGA X GA	A AAUCUUCA	UGAAGAUUU	GCGACUUU
3165 CUUAUAAA CUG 3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3169 GGUUCUUA CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3209 UUUAGGGG CUG 3210 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG	AUGA X GA	A AGUCGCAA	UUGCGACUU	UGGCCUGG
3167 UUCUUAUA CUG 3168 GUUCUUAU CUG 3169 GGUUCUUA CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3209 UUUAGGGG CUG 3210 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG	AUGA X GA	A AAGUCGCA	UGCGACUUU	GGCCUGGC
3168 GUUCUUAU CUG 3169 GGUUCUUA CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3209 UUUAGGGG CUG 3210 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG	auga x ga	A AUCCCGGG	CCCGGGAUA	UUUAU AA G
20 3169 GGUUCUUA CUG 3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3209 UUUAGGGG CUG 3210 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG	AUGA X GA	A AUAUCCCG	CGGGAUAUU	UAUAAGAA
3171 AGGGUUCU CUG 3183 CCUCACAU CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3204 GGGAAGUC CUG 3209 UUUAGGGG CUG 3210 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG	AUGA X GA	A AAUAUCCC	GGGAUAUUU	AUAAGAAC
3183 CCUCACAU CUG 3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3204 GGGAAGUC CUG 3209 UUUAGGGG CUG 3210 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG	AUGA X GA	A AAAUAUCC	GGAUAUUUA	UAAGAACC
3184 UCCUCACA CUG 3201 AAGUCGAG CUG 3204 GGGAAGUC CUG 3209 UUUAGGGG CUG 3210 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG	AUGA X GA	UAUAAAUA	AUAUUUAUA	AGAACCCU
3201 AAGUCGAG CUG 25 3204 GGGAAGUC CUG 3209 UUUAGGGG CUG 3210 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG	AUGA X GA	A AUCAGGGU	ACCCUGAUU	AUGUGAGG
25 3204 GGGAAGUC CUG 3209 UUUAGGGG CUG 3210 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG	AUGA X GA	A AAUCAGGG	CCCUGAUUA	UGUGAGGA
3209 UUUAGGG CUG 3210 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG	AUGA X GA	A AUCUCCUC	GAGGAGAUA	CUCGACUU
3210 UUUUAGGG CUG 3215 AUCCAUUU CUG 3228 GGAUUCAG CUG 30 3235 CAAAGAUG CUG	AUGA X GA	A AGUAUCUC	GAGAUACUC	GACUUCCC
3215 AUCCAUUU CUG 3228 GGAUUCAG CUG 30 3235 CAAAGAUG CUG	AUGA X GA	A AGUCGAGU	ACUCGACUU	CCCCUAAA
3228 GGAUUCAG CUG 30 3235 CAAAGAUG CUG	AUGA X GA	A AAGUCGAG	CUCGACUUC	CCCUAAAA
30 3235 CAAAGAUG CUG	AUGA X GA	A AGGGGAAG	CUUCCCCUA	AAAUGGAU
	AUGA X GA	A AGCCAUCC	GGAUGGCUC	CUGAAUCC
3239 UUGUCAAA CUG	AUGA X GA	A AUUCAGGA	UCCUGAAUC	CAUCUUUG
	AUGA X GA	A AUGGAUUC	GAAUCCAUC	UUUGACAA
3241 CCUUGUCA CUG	AUGA X GA	A AGAUGGAU	AUCCAUCUU	UGACAAGG
3242 ACCUUGUC CUG	AUGA X GA	A AAGAUGGA	UCCAUCUUU	GACAAGGU

	3251	GUGCUGUA	CUGAUGA	X	GAA	ACCUUGUC	GACAAGGUC	UACAGCAC
	3253	UGGUGCUG	CUGAUGA	X	GAA	AGACCUUG	CAAGGUCUA	CAGCACCA
	3277	CGCCAUAG	CUGAUGA	X	GAA	ACCACACA	UGUGUGGUC	CUAUGGCG
	3280	ACACGCCA	CUGAUGA	X	GAA	AGGACCAC	GUGGUCCUA	UGGCGUGU
5	3289	CCCACAGC	CUGAUGA	X	GAA	ACACGCCA	UGGCGUGUU	GCUGUGGG
	3302	AAGGAGAA	CUGAUGA	X	GAA	AUCUCCCA	UGGGAGAUC	uucuccuu
	3304	CUAAGGAG	CUGAUGA	X	GAA	AGAUCUCC	GGAGAUCUU	CUCCUUAG
	3305	CCUAAGGA	CUGAUGA	X	GAA	AAGAUCUC	GAGAUCUUC	UCCUUAGG
	3307	CCCCUAAG	CUGAUGA	X	GAA	AGAAGAUC	GAUCUUCUC	CUUAGGGG
10	3310	AACCCCCU	CUGAUGA	X	GAA	AGGAGAAG	cuucuccuu	AGGGGGUU
	3311	GAACCCCC	CUGAUGA	X	GAA	AAGGAGAA	UUCUCCUUA	GGGGGUUC
	3318	GUAUGGAG	CUGAUGA	X	GAA	ACCCCCUA	UAGGGGGUU	CUCCAUAC
	3319	GGUAUGGA	CUGAUGA	X	GAA	AACCCCCU	AGGGGGUUC	UCCAUACC
	3321	UGGGUAUG	CUGAUGA	X	GAA	AGAACCCC	GGGGUUCUC	CAUACCCA
15	3325	CUCCUGGG	CUGAUGA	X	GAA	AUGGAGAA	UUCUCCAUA	CCCAGGAG
	3352	GGCUGCAG	CUGAUGA	X	GAA	AGUCUUCA	UGAAGACUU	CUGCAGCC
	3353	CGGCUGCA	CUGAUGA	X	GAA	AAGUCUUC	GAAGACUUC	UGCAGCCG
	3397	GUGUGGCA	CUGAUGA	X	GAA	ACUCCGGG	CCCGGAGUA	UGCCACAC
	3413	AUUUGGUA	CUGAUGA	X	GAA	AUUUCAGG	CCUGAAAUC	UACCAAAU
20	3415	UGAUUUGG	CUGAUGA	X	GAA	AGAUUUCA	UGAAAUCUA	CCAAAUCA
	3422	UCCAACAU	CUGAUGA	X	GAA	AUUUGGUA	UACCAAAUC	AUGUUGGA
	3427	AGCAAUCC	CUGAUGA	X	GAA	ACAUGAUU	AAUCAUGUU	GGAUUGCU
	3432	GUGCCAGC	CUGAUGA	X	GAA	AUCCAACA	UGUUGGAUU	GCUGGCAC
	3466	GUUCAGCA	CUGAUGA	X	GAA	ACCGGGGC	GCCCCGGUU	UGCUGAAC
25	3467	AGUUCAGC	CUGAUGA	X	GAA	AACCGGGG	CCCCGGUUU	GCUGAACU
	3476	UUCUCCAC	CUGAUGA	X	GAA	AGUUCAGC	GCUGAACUU	GUGGAGAA
	3488	AGGUCACC	CUGAUGA	X	GAA	AGUUUCUC	GAGAAACUU	GGUGACCU
	3500	UUGGCUUG	CUGAUGA	X	GAA	AGCAGGUC	GACCUGCUU	CAAGCCAA
	3501	GUUGGCUU	CUGAUGA	X	GAA	AAGCAGGU	ACCUGCUUC	AAGCCAAC
30	3512	UCCUGUUG	CUGAUGA	X	GAA	ACGUUGGC	GCCAACGUC	CAACAGGA
	3531	GGGGAUGU	CUGAUGA	X	GAA	AUCUUUCC	GGAAAGAUU 2	ACAUCCCC
	3532	GGGGGAUG	CUGAUGA	X	GAA	AAUCUUUC	GAAAGAUUA	CAUCCCCC
	3536	UUGAGGGG	CUGAUGA	X	GAA	AUGUAAUC	GAUUACAUC	CCCCUCAA

	3542	AUGGCAUU	CUGAUGA	X	GAA	AGGGGGAU	AUCCCCCUC	AAUGCCAU
	3551	CUAGUCAG	CUGAUGA	X	GAA	AUGGCAUU	AAUGCCAUA	CUGACUAG
	3558	ACUGUUUC	CUGAUGA	X	GAA	AGUCAGUA	UACUGACUA	GAAACAGU
	3567	UGUGAAGC	CUGAUGA	X	GAA	ACUGUUUC	GAAACAGUA	GCUUCACA
5	3571	AGUAUGUG	CUGAUGA	X	GAA	AGCUACUG	CAGUAGCUU	CACAUACU
	3572	GAGUAUGU	CUGAUGA	X	GAA	AAGCUACU	AGUAGCUUC	ACAUACUC
	3577	GGGUCGAG	CUGAUGA	X	GAA	AUGUGAAG	CUUCACAUA	CUCGACCC
	3580	UGGGGGUC	CUGAUGA	X	GAA	AGUAUGUG	CACAUACUC	GACCCCCA
	3592	CCUCAGAG	CUGAUGA	X	GAA	AGGUGGGG	CCCCACCUU	CUCUGAGG
10	35 93	UCCUCAGA	CUGAUGA	X	GAA	AAGGUGGG	CCCACCUUC	UCUGAGGA
	3 5 95	GGUCCUCA	CUGAUGA	X	GAA	AGAAGGUG	CACCUUCUC	UGAGGACC
	3605	UCCUUGAA	CUGAUGA	X	GAA	AGGUCCUC	GAGGACCUU	UUCAAGGA
	3606	GUCCUUGA	CUGAUGA	X	GAA	AAGGUCCU	AGGACCUUU	UCAAGGAC
	3607	CGUCCUUG	CUGAUGA	X	GAA	AAAGGUCC	GGACCUUUU	CAAGGACG
15	3608	CCGUCCUU	CUGAUGA	X	GAA	AAAAGGUC	GACCUUUUC	AAGGACGG
	3619	GAUCUGCA	CUGAUGA	X	GAA	AGCCGUCC	GGACGGCUU	UGCAGAUC
	3620	GGAUCUGC	CUGAUGA	X	GAA	AAGCCGUC	GACGGCUUU	GCAGAUCC
	3627	AAAAUGUG	CUGAUGA	X	GAA	AUCUGCAA	UUGCAGAUC	CACAUUUU
	363 3	GGAAUGAA	CUGAUGA	X	GAA	AUGUGGAU	AUCCACAUU	UUCAUUCC
20	3634	CGGAAUGA	CUGAUGA	X	GAA	AAUGUGGA	UCCACAUUU	UCAUUCCG
	36 35	CCGGAAUG	CUGAUGA	X	GAA	AAAUGUGG	CCACAUUUU	CAUUCCGG
	3636					AAAAUGUG	CACAUUUUC	AUUCCGGA
	3639	GCUUCCGG	CUGAUGA	X	GAA	AUGAAAAU	AUUUUCAUU	CCGGAAGC
	3640	AGCUUCCG	CUGAUGA	X	GAA	AAUGAAAA	UUUUCAUUC	CGGAAGCU
25	3649					AGCUUCCG		
	3664						UGUGAGAUA	
	3668						AGAUAUGUA	
	3675						UAAACGCUU	
	3 6 76						AAACGCUUU	CAAAUUCA
30	3677					AAAGCGUU		AAAUUCAU
	3682					AUUUGAAA		
	3683						UUCAAAUUC	
	3701	AAGGUUUU	CUGAUGA	Х	GAA	AUUCUUUC	GAAAGAAUC	AAAACCUU

	3709	GCUCCUCA	CUGAUGA	X	GAA	AGGUUUUG	CAAAACCUU	UGAGGAGC
	3710	AGCUCCUC	CUGAUGA	X	GAA	AAGGUUUU	AAAACCUUU	GAGGAGCU
	3719	UUCGGUGA	CUGAUGA	X	GAA	AGCUCCUC	GAGGAGCUU	UCACCGAA
	3720	GUUCGGUG	CUGAUGA	X	GAA	AAGCUCCU	AGGAGCUUU	CACCGAAC
5	3721	AGUUCGGU	CUGAUGA	X	GAA	AAAGCUCC	GGAGCUUUC	ACCGAACU
	3730	UGGAGGUG	CUGAUGA	X	GAA	AGUUCGGU	ACCGAACUC	CACCUCCA
	3736	CAAACAUG	CUGAUGA	X	GAA	AGGUGGAG	CUCCACCUC	CAUGUUUG
	3742	AGUCCUCA	CUGAUGA	X	GAA	ACAUGGAG	CUCCAUGUU	UGAGGACU
	3743	UAGUCCUC	CUGAUGA	X	GAA	AACAUGGA	UCCAUGUUU	GAGGACUA
10	3751	CCAGCUGA	CUGAUGA	X	GAA	AGUCCUCA	UGAGGACUA	UCAGCUGG
	3753	GUCCAGCU	CUGAUGA	X	GAA	AUAGUCCU	AGGACUAUC	AGCUGGAC
	3765	CAGAGUGC	CUGAUGA	X	GAA	AGUGUCCA	UGGACACUA	GCACUCUG
	3771	GCCCAGCA	CUGAUGA	X	GAA	AGUGCUAG	CUAGCACUC	UGCUGGGC
	3781	GCAAGGGG	CUGAUGA	X	GAA	AGCCCAGC	GCUGGGCUC	CCCCUUGC
15	3787	GCUUCAGC	CUGAUGA	X	GAA	AGGGGGAG	cucccccuu	GCUGAAGC
	3799	UCCAGGUG	CUGAUGA	X	GAA	ACCGCUUC	GAAGCGGUU	CACCUGGA
	3800	GUCCAGGU	CUGAUGA	X	GAA	AACCGCUU	AAGCGGUUC	ACCUGGAC
	3829	UCUUCAUG	CUGAUGA	X	GAA	AGGCCUUG	CAAGGCCUC	CAUGAAGA
	3839	CUCAAGUC	CUGAUGA	X	GAA	AUCUUCAU	AUGAAGAUA	GACUUGAG
20	3844	CUAUUCUC	CUGAUGA	X	GAA	AGUCUAUC	GAUAGACUU	GAGAAUAG
	3851	UUACUCGC	CUGAUGA	X	GAA	AUUCUCAA	UUGAGAAUA	GCGAGUAA
	3858	CUUGCUUU	CUGAUGA	X	GAA	ACUCGCUA	UAGCGAGUA	AAAGCAAG
	3878	AGAUCGGA	CUGAUGA	X	GAA	AGUCCCGC	GCGGGACUU	UCCGAUCU
	3879	CAGAUCGG	CUGAUGA	X	GAA	AAGUCCCG	CGGGACUUU	CCGAUCUG
25	3880	GCAGAUCG	CUGAUGA	X	GAA	AAAGUCCC	GGGACUUUC	CGAUCUGC
	3885	CCUCGGCA	CUGAUGA	X	GAA	AUCGGAAA	UUUCCGAUC	UGCCGAGG
	3901	AGAAGCAG	CUGAUGA	X	GAA	AGCUGGGC	GCCCAGCUU	CUGCUUCU
	3902	GAGAAGCA	CUGAUGA	X	GAA	AAGCUGGG	CCCAGCUUC	UGCUUCUC
	3907	AGCUGGAG	CUGAUGA	X	GAA	AGCAGAAG	CUUCUGCUU	CUCCAGCU
30	3908	CAGCUGGA	CUGAUGA	X	GAA	AAGCAGAA	UUCUGCUUC	UCCAGCUG
	391 0	CACAGCUG	CUGAUGA	X	GAA	AGAAGCAG	CUGCUUCUC	CAGCUGUG
	3926	ACGGGCCU	CUGAUGA	X	GAA	AUGUGGCC	GGCCACAUC	AGGCCCGU
	3949	CCAGCUCA	CUGAUGA	X	GAA	AUUCAUCG	CGAUGAAUC	UGAGCUGG

	3967	AACAGCAG	CUGAUGA	X	GAA	ACUCCUUU	AAAGGAGUC	CUGCUGUU
	3975	GGGUGGAG	CUGAUGA	X	GAA	ACAGCAGG	CCUGCUGUU	CUCCACCC
	3976	GGGGUGGA	CUGAUGA	X	GAA	AACAGCAG	CUGCUGUUC	UCCACCCC
	3978	UGGGGGUG	CUGAUGA	X	GAA	AGAACAGC	GCUGUUCUC	CACCCCCA
5	3991	CGGAGUUG	CUGAUGA	X	GAA	AGUCUGGG	CCCAGACUA	CAACUCCG
	3997	ACACCACG	CUGAUGA	X	GAA	AGUUGUAG	CUACAACUC	CGUGGUGU
	4006	AGGAGUAC	CUGAUGA	X	GAA	ACACCACG	CGUGGUGUU	GUACUCCU
	4009	GGGAGGAG	CUGAUGA	X	GAA	ACAACACC	GGUGUUGUA	CUCCUCCC
	4012	GCGGGGAG	CUGAUGA	X	GAA	AGUACAAC	GUUGUACUC	CUCCCCGC
10	4015	CGGCGGG	CUGAUGA	X	GAA	AGGAGUAC	GUACUCCUC	CCCGCCCG
	4027	AGAAGCUU	CUGAUGA	X	GAA	AGGCGGGC	GCCCGCCUA	AAGCUUCU
	4033	CUGGUGAG	CUGAUGA	X	GAA	AGCUUUAG	CUAAAGCUU	CUCACCAG
	4034	GCUGGUGA	CUGAUGA	X	GAA	AAGCUUUA	UAAAGCUUC	UCACCAGC
	4036	GGGCUGGU	CUGAUGA	X	GAA	AGAAGCUU	AAGCUUCUC	ACCAGCCC
15	4066	AUGUAUAA	CUGAUGA	X	GAA	ACUGUCAG	CUGACAGUA	UUAUACAU
	4068	AGAUGUAU	CUGAUGA	X	GAA	AUACUGUC	GACAGUAUU	AUACAUCU
	4069	UAGAUGUA	CUGAUGA	X	GAA	AAUACUGU	ACAGUAUUA	UACAUCUA
	4071	CAUAGAUG	CUGAUGA	X	GAA	AUAAUACU	AGUAUUAUA	CAUCUAUG
	4075	AACUCAUA	CUGAUGA	X	GAA	AUGUAUAA	UUAUACAUC	UAUGAGUU
20	4077	UAAACUCA	CUGAUGA	X	GAA	AGAUGUAU	AUACAUCUA	UGAGUUUA
	4083	UAGGUGUA	CUGAUGA	X	GAA	ACUCAUAG	CUAUGAGUU	UACACCUA
	4084	AUAGGUGU	CUGAUGA	X	GAA	AACUCAUA	UAUGAGUUU	ACACCUAU
	4085	AAUAGGUG	CUGAUGA	X	GAA	AAACUCAU	AUGAGUUUA	CACCUAUU
	4091	GAGCGGAA	CUGAUGA	X	GAA	AGGUGUAA	UUACACCUA	UUCCGCUC
25	4093	UGGAGCGG	CUGAUGA	X	GAA	AUAGGUGU	ACACCUAUU	CCGCUCCA
	4094	GUGGAGCG	CUGAUGA	X	GAA	AAUAGGUG	CACCUAUUC	CGCUCCAC
	4099	CUCCUGUG	CUGAUGA	X	GAA	AGCGGAAU	AUUCCGCUC	CACAGGAG
	4117	GUCACGAA	CUGAUGA	X	GAA	AGCAGCUG	CAGCUGCUU	UUCGUGAC
	4118	GGUCACGA	CUGAUGA	X	GAA	AAGCAGCU	AGCUGCUUU	UCGUGACC
30	4119	AGGUCACG	CUGAUGA	X	GAA	AAAGCAGC	GCUGCUUUU	CGUGACCU
	4120					AAAAGCAG		
	4128	CACGAUUA	CUGAUGA	X	GAA	AGGUCACG	CGUGACCUU	UAAUCGUG
	4129	GCACGAUU	CUGAUGA	X	GAA	AAGGUCAC	GUGACCUUU	AAUCGUGC

	4130	AGCACGAU	CUGAUGA	x	GAA	AAAGGUCA	UGACCUUUA	AUCGUGCU
	4133	AAAAGCAC	CUGAUGA	X	GAA	AUUAAAGG	CCUUUAAUC	GUGCUUUU
	4139	AAACAAAA	CUGAUGA	x	GAA	AGCACGAU	AUCGUGCUU	บบบบเรบบบ
	4140	AAAACAAA	CUGAUGA	X	GAA	AAGCACGA	UCGUGCUUU	UUUGUUUU
5	4141	AAAAACAA	CUGAUGA	X	GAA	AAAGCACG	CGUGCUUUU	UUGUUUUU
	4142	AAAAAACA	CUGAUGA	X	GAA	AAAAGCAC	GUGCUUUUU	บดบบบบบบ
	4143	CAAAAAAC	CUGAUGA	X	GAA	AAAAAGCA	UGCUUUUUU	GUUUUUUG
	4146	AAACAAAA	CUGAUGA	X	GAA	ACAAAAA	บบบบบบน	บบบบเรบบบ
	4147	AAAACAAA	CUGAUGA	X	GAA	AACAAAA	บบบบบฐบบบ	บบบเรียบบบบ
10	4148	CAAAACAA	CUGAUGA	X	GAA	AAACAAAA	บบบบเดิบบบบ	UUGUUUUG
	4149	ACAAAACA	CUGAUGA	X	GAA	AAAACAAA	UUUGUUUUU	UGUU UU GU
	4150	AACAAAAC	CUGAUGA	X	GAA	AAAAACAA	บบเดินบบบบบ	GUUUUGUU
	4153	ACAAACAA	CUGAUGA	X	GAA	ACAAAAA	UUUUUUGUU	UUGUUUGU
	4154	AACAAACA	CUGAUGA	X	GAA	AACAAAAA	UUUUUGUUU	UGUUUGUU
15	4155	CAACAAAC	CUGAUGA	X	GAA	AAACAAAA	บบบบเริบบบบ	GUUUGUUG
	4158	CAACAACA	CUGAUGA	X	GAA	ACAAAACA	UGUUUUGUU	UGUUGUUG
	4159	GCAACAAC	CUGAUGA	X	GAA	AACAAAAC	GUUUUGUUU	GUUGUUGC
	4162	ACAGCAAC	CUGAUGA	X	GAA	ACAAACAA	UUGUUUGUU	GUUGCUGU
	4165	AAAACAGC	CUGAUGA	X	GAA	ACAACAAA	UUUGUUGUU	GCUGUUUU
20	4171	UUAGUCAA	CUGAUGA	X	GAA	ACAGCAAC	GUUGCUGUU	UUGACUAA
	4172	GUUAGUCA	CUGAUGA	X	GAA	AACAGCAA	UUGCUGUUU	UGACUAAC
	4173	UGUUAGUC	CUGAUGA	X	GAA	AAACAGCA	UGCUGUUUU	GACUAACA
	4178	AUUCUUGU	CUGAUGA	X	GAA	AGUCAAAA	UUUUGACUA	ACAAGAAU
	4189	ACUGGGGU	CUGAUGA	X	GAA	ACAUUCUU	AAGAAUGUA	ACCCCAGU
25	4198	ACGUCACU	CUGAUGA	X	GAA	ACUGGGGU	ACCCCAGUU	AGUGACGU
	4199	CACGUCAC	CUGAUGA	X	GAA	AACUGGGG	CCCCAGUUA	GUGACGUG
	4216	AACAAUAG	CUGAUGA	X	GAA	AUUCUUCA	UGAAGAAUA	CUAUUGUU
	4219	UCUAACAA	CUGAUGA	X	GAA	AGUAUUCU	AGAAUACUA	UUGUUAGA
	4221	UCUCUAAC	CUGAUGA	X	GAA	AUAGUAUU	AAUACUAUU	GUUAGAGA
30	4224	AUUUCUCU	CUGAUGA	X	GAA	ACAAUAGU	ACUAUUGUU	AGAGAAAU
	4225	GAUUUCUC	CUGAUGA	X	GAA	AACAAUAG	CUAUUGUUA	GAGAAAUC
	4233	GCGGGGG	CUGAUGA	X	GAA	AUUUCUCU	AGAGAAAUC	CCCCCCCC
	4249	GUUACCCU	CUGAUGA	X	GAA	AGGCUUUG	CAAAGCCUC	AGGGUAAC

	4255	GUCCAGGU	CUGAUGA	Х	GAA	ACCCUGAG	CUCAGGGUA	ACCUGGAC
	4282	GGUCGCCA	CUGAUGA	X	GAA	AGGCACCU	AGGUGCCUC	UGGCGACC
	4323	GCUGCAGG	CUGAUGA	X	GAA	AGGGUGGG	CCCACCCUC	CCUGCAGC
	4341	ACUGCCUC	CUGAUGA	X	GAA	AGUCCCAC	GUGGGACUA	GAGGCAGU
5	4350	AAUGGGCU	CUGAUGA	X	GAA	ACUGCCUC	GAGGCAGUA	AGCCCAUU
	4358	CAUGAGCU	CUGAUGA	X	GAA	AUGGGCUU	AAGCCCAUU	AGCUCAUG
	4359	CCAUGAGC	CUGAUGA	X	GAA	AAUGGGCU	AGCCCAUUA	GCUCAUGG
	4363	GCAGCCAU	CUGAUGA	X	GAA	AGCUAAUG	CAUUAGCUC	AUGGCUGC
	4387	GAGAGACA	CUGAUGA	X	GAA	AGCAGGUC	GACCUGCUC	ugucucuc
10	4391	AUAAGAGA	CUGAUGA	X	GAA	ACAGAGCA	UGCUCUGUC	UCUCUUAU
	4393	CCAUAAGA	CUGAUGA	X	GAA	AGACAGAG	CUCUGUCUC	UCUUAUGG
	4395	CUCCAUAA	CUGAUGA	X	GAA	AGAGACAG	CUGUCUCUC	UUAUGGAG
	4397	UCCUCCAU	CUGAUGA	X	GAA	AGAGAGAC	GUCUCUCUU	AUGGAGGA
	4398	UUCCUCCA	CUGAUGA	X	GAA	AAGAGAGA	UCUCUCUUA	UGGAGGAA
15	4445	GCAUCCCA	CUGAUGA	X	GAA	AGCCUUUU	AAAAGGCUU	UGGGAUGC
	4446	CGCAUCCC	CUGAUGA	X	GAA	AAGCCUUU	AAAGGCUUU	GGGAUGCG
	4456	ACAGGACG	CUGAUGA	X	GAA	ACGCAUCC	GGAUGCGUC	CGUCCUGU
	4460	CUCCACAG	CUGAUGA	X	GAA	ACGGACGC	GCGUCCGUC	CUGUGGAG
	4487	GCAUAGCG	CUGAUGA	X	GAA	AGCCCCCU	AGGGGGCUC	CGCUAUGC
20	4492	AAGUGGCA	CUGAUGA	X	GAA	AGCGGAGC	GCUCCGCUA	UGCCACUU
	4500	AGUCACUG	CUGAUGA	X	GAA	AGUGGCAU	AUGCCACUU	CAGUGACU
	4501	AAGUCACU	CUGAUGA	X	GAA	AAGUGGCA	UGCCACUUC	AGUGACUU
	4509	GGAGUGAG	CUGAUGA	X	GAA	AGUCACUG	CAGUGACUU	CUCACUCC
	4510	AGGAGUGA	CUGAUGA	X	GAA	AAGUCACU	AGUGACUUC	UCACUCCU
2 5	4512	CCAGGAGU	CUGAUGA	X	GAA	AGAAGUCA	UGACUUCUC	ACUCCUGG
	4516	GAGGCCAG	CUGAUGA	X	GAA	AGUGAGAA	UUCUCACUC	CUGGCCUC
	4524	AAACAGCG	CUGAUGA	X	GAA	AGGCCAGG	CCUGGCCUC	CGCUGUUU
	4531	GGGCCCGA	CUGAUGA	X	GAA	ACAGCGGA	UCCGCUGUU	UCGGGCCC
	4532	GGGGCCCG	CUGAUGA	X	GAA	AACAGCGG	CCGCUGUUU	CGGGCCCC
30	4533	GGGGCCC	CUGAUGA	X	GAA	AAACAGCG	CGCUGUUUC	GGGCCCCC
	4543	CCUCUUGG	CUGAUGA	X	GAA	AGGGGGCC	GGCCCCCUU	CCAAGAGG
	4544	ACCUCUUG	CUGAUGA	X	GAA	AAGGGGGC	GCCCCCUUC	CAAGAGGU
	4553	UGCUCUGA	CUGAUGA	X	GAA	ACCUCUUG	CAAGAGGUA	UCAGAGCA

	4555	ucugcucu	CUGAUGA	X	GAA	AUACCUCU	AGAGGUAUC	AGAGCAGA
	4577	GUCUAGGA	CUGAUGA	X	GAA	ACGUCCCU	AGGGACGUU	UCCUAGAC
	4578	GGUCUAGG	CUGAUGA	X	GAA	AACGUCCC	GGGACGUUU	CCUAGACC
	4579	UGGUCUAG	CUGAUGA	X	GAA	AAACGUCC	GGACGUUUC	CUAGACCA
5	4582	CCCUGGUC	CUGAUGA	X	GAA	AGGAAACG	CGUUUCCUA	GACCAGGG
	4598	UUCCCGAG	CUGAUGA	x	GAA	ACAUGUGC	GCACAUGUU	CUCGGGAA
	4599	GUUCCCGA	CUGAUGA	X	GAA	AACAUGUG	CACAUGUUC	UCGGGAAC
	4601	UGGUUCCC	CUGAUGA	X	GAA	AGAACAUG	CAUGUUCUC	GGGAACCA
	4614	UUAAGAUU	CUGAUGA	X	GAA	ACUGUGGU	ACCACAGUU	AAUCUUAA
10	4615	UUUAAGAU	CUGAUGA	X	GAA	AACUGUGG	CCACAGUUA	AUCUUAAA
	4618	AGAUUUAA	CUGAUGA	X	GAA	AUUAACUG	CAGUUAAUC	UUAAAUCU
	4620	AAAGAUUU	CUGAUGA	X	GAA	AGAUUAAC	GUUAAUCUU	AAAUCUUU
	4621	AAAAGAUU	CUGAUGA	X	GAA	AAGAUUAA	UUAAUCUUA	AAUCUUUU
	4625	CGGGAAAA	CUGAUGA	X	GAA	AUUUAAGA	UCUUAAAUC	UUUUCCCG
15	4627	CCCGGGAA	CUGAUGA	X	GAA	AGAUUUAA	UUAAAUCUU	UUCCCGGG
	4628	UCCCGGGA	CUGAUGA	X	GAA	AAGAUUUA	UAAAUCUUU	UCCCGGGA
	4629	CUCCCGGG	CUGAUGA	X	GAA	AAAGAUUU	AAAUCUUUU	CCCGGGAG
	4630	ACUCCCGG	CUGAUGA	X	GAA	AAAAGAUU	AAUCUUUUC	CCGGGAGU
	4639	CAACAGAA	CUGAUGA	X	GAA	ACUCCCGG	CCGGGAGUC	UUCU GUU G
20	4641	GACAACAG	CUGAUGA	X	GAA	AGACUCCC	GGGAGUCUU	CUGUUGUC
	4642	AGACAACA	CUGAUGA	X	GAA	AAGACUCC	GGAGUCUUC	UGUUGUCU
	464 6	AAACAGAC	CUGAUGA	X	GAA	ACAGAAGA	UCUUCUGUU	GUCUGUUU
	4649	GGUAAACA	CUGAUGA	X	GAA	ACAACAGA	UCUGUUGUC	UGUUUACC
	46 53	GGAUGGUA	CUGAUGA	X	GAA	ACAGACAA	UUGUCUGUU	UACCAUCC
25	4654	UGGAUGGU	CUGAUGA	X	GAA	AACAGACA	UGUCUGUUU	ACCAUCCA
	4655	UUGGAUGG	CUGAUGA	X	GAA	AAACAGAC	GUCUGUUUA	CCAUCCAA
	46 60	AUGCUUUG	CUGAUGA	X	GAA	AUGGUAAA	UUUACCAUC	CAAAGCAU
	46 69	AUGUUAAA	CUGAUGA	X	GAA	AUGCUUUG	CAAAGCAUA	UUUAACAU
	4671	ACAUGUUA	CUGAUGA	X	GAA	AUAUGCUU	AAGCAUAUU	UAACAUGU
30	4672	CACAUGUU	CUGAUGA	X	GAA	AAUAUGCU	AGCAUAUUU	AACAUGUG
	4673	ACACAUGU	CUGAUGA	X	GAA	AAAUAUGC	GCAUAUUUA	ACAUGUGU
	4682	CCCCCACU	CUGAUGA	X	GAA	ACACAUGU	ACAUGUGUC	AGUGGGGG
	4698	CAGAAGCC	CUGAUGA	X	GAA	AGCGCCAC	GUGGCGCUU	GGCUUCUG

	4703	GGCCUCAG	CUGAUGA	X	GAA	AGCCAAGC	GCUUGGCUU CUGAGGCC
	4704	UGGCCUCA	CUGAUGA	X	GAA	AAGCCAAG	CUUGGCUUC UGAGGCCA
	4720	GAACUGAU	CUGAUGA	X	GAA	AUGGCUCU	AGAGCCAUC AUCAGUUC
	4723	GAGGAACU	CUGAUGA	X	GAA	AUGAUGGC	GCCAUCAUC AGUUCCUC
5	4727	ACUAGAGG	CUGAUGA	X	GAA	ACUGAUGA	UCAUCAGUU CCUCUAGU
	4728	CACUAGAG	CUGAUGA	X	GAA	AACUGAUG	CAUCAGUUC CUCUAGUG
	4731	UCUCACUA	CUGAUGA	X	GAA	AGGAACUG	CAGUUCCUC UAGUGAGA
	4733	CAUCUCAC	CUGAUGA	X	GAA	AGAGGAAC	GUUCCUCUA GUGAGAUG
	4745	AUGACCUC	CUGAUGA	X	GAA	AUGCAUCU	AGAUGCAUU GAGGUCAU
10	4751	UUGGGUAU	CUGAUGA	X	GAA	ACCUCAAU	AUUGAGGUC AUACCCAA
	4754	AGCUUGGG	CUGAUGA	X	GAA	AUGACCUC	GAGGUCAUA CCCAAGCU
	4763	AGGCCUGC	CUGAUGA	X	GAA	AGCUUGGG	CCCAAGCUU GCAGGCCU
	4777	AGUAUGCG	CUGAUGA	X	GAA	AGGUCAGG	CCUGACCUU CGCAUACU
	4778	CAGUAUGC	CUGAUGA	X	GAA	AAGGUCAG	CUGACCUUC GCAUACUG
15	4783	GUGAGCAG	CUGAUGA	Χ.	GAA	AUGCGAAG	CUUCGCAUA CUGCUCAC
	4789	CUCCCCGU	CUGAUGA	X	GAA	AGCAGUAU	AUACUGCUC ACGGGGAG
	4799	GACCACUU	CUGAUGA	X	GAA	ACUCCCCG	CGGGGAGUU AAGUGGUC
	4800	GGACCACU	CUGAUGA	X	GAA	AACUCCCC	GGGGAGUUA AGUGGUCC
	4807	CCAAACUG	CUGAUGA	X	GAA	ACCACUUA	UAAGUGGUC CAGUUUGG
20	4812	CUAGGCCA	CUGAUGA	X	GAA	ACUGGACC	GGUCCAGUU UGGCCUAG
	4813	ACUAGGCC	CUGAUGA	X	GAA	AACUGGAC	GUCCAGUUU GGCCUAGU
	4819	AACCUUAC	CUGAUGA	X	GAA	AGGCCAAA	UUUGGCCUA GUAAGGUU
	4822	GGCAACCU	CUGAUGA	X	GAA	ACUAGGCC	GGCCUAGUA AGGUUGCC
	4827	CAGUAGGC	CUGAUGA	X	GAA	ACCUUACU	AGUAAGGUU GCCUACUG
25	4832	CCCAUCAG	CUGAUGA	X	GAA	AGGCAACC	GGUUGCCUA CUGAUGGG
	4843	UGGCUUUU	CUGAUGA	X	GAA	AGCCCAUC	GAUGGGCUC AAAAGCCA
	4855	CUGUUUAA	CUGAUGA	X	GAA	AUGUGGCU	AGCCACAUU UUAAACAG
	4856	CCUGUUUA	CUGAUGA	X	GAA	AAUGUGGC	GCCACAUUU UAAACAGG
	4857	ACCUGUUU	CUGAUGA	X	GAA	AAAUGUGG	CCACAUUUU AAACAGGU
30	4858	AACCUGUU	CUGAUGA	X	GAA	AAAAUGUG	CACAUUUUA AACAGGUU
	4866	UGAGAUAA	CUGAUGA	X	GAA	ACCUGUUU	AAACAGGUU UUAUCUCA
	4867	UUGAGAUA	CUGAUGA	X	GAA	AACCUGUU	AACAGGUUU UAUCUCAA
	4868	CUUGAGAU	CUGAUGA	X	GAA	AAACCUGU	ACAGGUUUU AUCUCAAG

	4869	ACUUGAGA	CUGAUGA	X	GAA	AAAACCUG	CAGGUUUUA	UCUCAAGU
	4871	AUACUUGA	CUGAUGA	X	GAA	AUAAAACC	GGUUUUAUC	UCAAGUAU
	4873	UAAUACUU	CUGAUGA	X	GAA	AGAUAAAA	UUUUAUCUC	AAGUAUUA
	4878	AAUUAUAA	CUGAUGA	X	GAA	ACUUGAGA	UCUCAAGUA	UUAAUAUA
5	4880	UAUAUAUU	CUGAUGA	X	GAA	AUACUUGA	UCAAGUAUU	AAUAUAUA
	4881	CUAUAUAU	CUGAUGA	X	GAA	AAUACUUG	CAAGUAUUA	AUAUAUAG
	4884	UGUCUAUA	CUGAUGA	X	GAA	AUUAAUAC	GUAUUAAUA	UAUAGACA
	488 6	CUUGUCUA	CUGAUGA	X	GAA	AUAUUAAU	AUUAAUAUA	UAGACAAG
	4888	GUCUUGUC	CUGAUGA	X	GAA	AUAUAUUA	UAAUAUAUA	GACAAGAC
10	4900	UAAUGCAU	CUGAUGA	X	GAA	AGUGUCUU	AAGACACUU	AUGCAUUA
	4901	AUAAUGCA	CUGAUGA	X	GAA	AAGUGUCU	AGACACUUA	UGCAUUAU
	4907	AACAGGAU	CUGAUGA	X	GAA	AUGCAUAA	UUAUGCAUU	AUCCUGUU
	4908	AAACAGGA	CUGAUGA	X	GAA	AAUGCAUA	UAUGCAUUA	UCCUGUUU
	4910	UAAAACAG	CUGAUGA	X	GAA	AUAAUGCA	UGCAUUAUC	CUGUUUUA
15	4915	AUAUAUAA	CUGAUGA	x	GAA	ACAGGAUA	UAUCCUGUU	UUAUAUAU
	4916	GAUAUAUA	CUGAUGA	X	GAA	AACAGGAU	AUCCUGUUU	UAUAUAUC
	4917	GGAUAUAU	CUGAUGA	X	GAA	AAACAGGA	uccuguuuu	AUAUAUCC
	4918	UGGAUAUA	CUGAUGA	X	GAA	AAAACAGG	CCUGUUUUA	UAUAUCCA
	4920	AUUGGAUA	CUGAUGA	X	GAA	AUAAAACA	UGUUUUAUA	UAUCCAAU
20	4922	UCAUUGGA	CUGAUGA	X	GAA	AUAUAAAA	AUAUAUUU	UCCAAUGA
	4924	AUUCAUUG	CUGAUGA	x	GAA	AUAUAUAA	UUAUAUAUC	CAAUGAAU
	4933	CCCAGUUA	CUGAUGA	x	GAA	AUUCAUUG	CAAUGAAUA	UAACUGGG
	4935	GCCCCAGU	CUGAUGA	X	GAA	AUAUUCAU	AUGAAUAUA	ACUGGGGC
	4948	UGACUCUU	CUGAUGA	X	GAA	ACUCGCCC	GGGCGAGUU	AAGAGUCA
25	4949	AUGACUCU	CUGAUGA	X	GAA	AACUCGCC	GGCGAGUUA	AGAGUCAU
	4955	UAGACCAU	CUGAUGA	X	GAA	ACUCUUAA	UUAAGAGUC	AUGGUCUA
	4961	CUUUUCUA	CUGAUGA	X	GAA	ACCAUGAC	GUCAUGGUC	UAGAAAAG
	4963	cccuuuuc	CUGAUGA	X	GAA	AGACCAUG	CAUGGUCUA	GAAAAGGG
	4974	UACAGAGA	CUGAUGA	X	GAA	ACCCCUUU	AAAGGGGUU	UCUCUGUA
30	4975	GUACAGAG	CUGAUGA	X	GAA	AACCCCUU	AAGGGGUUU	CUCUGUAC
	497 6	GGUACAGA	CUGAUGA	X	GAA	AAACCCCU	AGGGGUUUC	UCUGUACC
	4978	UGGGUACA	CUGAUGA	X	GAA	AGAAACCC	GGGUUUCUC	UGUACCCA
	4982	GAUUUGGG	CUGAUGA	X	GAA	ACAGAGAA	UUCUCUGUA	CCCAAAUC

	4990	ACCAGCCC	CUGAUGA	X	GAA	AUUUGGGU	ACCCAAAUC GGGCUGGU
	4999	CUUGGUCC	CUGAUGA	X	GAA	ACCAGCCC	GGGCUGGUU GGACCAAG
	5029	GCUGGGAC	CUGAUGA	X	GAA	ACCACUCU	AGAGUGGUU GUCCCAGC
	5032	AUAGCUGG	CUGAUGA	X	GAA	ACAACCAC	GUGGUUGUC CCAGCUAU
5	5039	AGUAACUA	CUGAUGA	X	GAA	AGCUGGGA	UCCCAGCUA UAGUUACU
	5041	UUAGUAAC	CUGAUGA	X	GAA	AUAGCUGG	CCAGCUAUA GUUACUAA
	5044	AGUUUAGU	CUGAUGA	X	GAA	ACUAUAGC	GCUAUAGUU ACUAAACU
	5045	UAGUUUAG	CUGAUGA	X	GAA	AACUAUAG	CUAUAGUUA CUAAACUA
	5048	GAGUAGUU	CUGAUGA	X	GAA	AGUAACUA	UAGUUACUA AACUACUC
10	505 3	UGGGUGAG	CUGAUGA	X	GAA	AGUUUAGU	ACUAAACUA CUCACCCA
	5056	CUUUGGGU	CUGAUGA	X	GAA	AGUAGUUU	AAACUACUC ACCCAAAG
	5066	GAGGUCCC	CUGAUGA	X	GAA	ACUUUGGG	CCCAAAGUU GGGACCUC
	5074	AAGCCAGU	CUGAUGA	X	GAA	AGGUCCCA	UGGGACCUC ACUGGCUU
	5082	GUAAAGAG	CUGAUGA	X	GAA	AGCCAGUG	CACUGGCUU CUCUUUAC
15	508 3	AGUAAAGA	CUGAUGA	X	GAA	AAGCCAGU	ACUGGCUUC UCUUUACU
	5085	GAAGUAAA	CUGAUGA	X	GAA	AGAAGCCA	UGGCUUCUC UUUACUUC
	5087	AUGAAGUA	CUGAUGA	X	GAA	AGAGAAGC	GCUUCUCUU UACUUCAU
	5088	GAUGAAGU	CUGAUGA	X	GAA	AAGAGAAG	CUUCUCUUU ACUUCAUC
	5089	UGAUGAAG	CUGAUGA	X	GAA	AAAGAGAA	UUCUCUUUA CUUCAUCA
20	5092	CCAUGAUG	CUGAUGA	X	GAA	AGUAAAGA	UCUUUACUU CAUCAUGG
	509 3	UCCAUGAU	CUGAUGA	Х	GAA	AAGUAAAG	CUUUACUUC AUCAUGGA
	509 6	AAAUCCAU	CUGAUGA	X	GAA	AUGAAGUA	UACUUCAUC AUGGAUUU
	510 3					AUCCAUGA	UCAUGGAUU UCACCAUC
							CAUGGAUUU CACCAUCC
25							AUGGAUUUC ACCAUCCC
							UUCACCAUC CCAAGGCA
							AAGGCAGUC UGAGAGGA
	5134						GAGGAGCUA AAGAGUAU
	5141						UAAAGAGUA UCAGCCCA
30	5143						AAGAGUAUC AGCCCAUA
							CAGCCCAUA UUUAUUAA
							GCCCAUAUU UAUUAAGC
	5154	UGCUUAAU	CUGAUGA	X	GAA	AAUAUGGG	CCCAUAUUU AUUAAGCA

	5155	GUGCUUAA	CUGAUGA	X	GAA	AAAUAUGG	CCAUAUUUA	UUAAGCAC
	5157	AAGUGCUU	CUGAUGA	X	GAA	AUAAAUAU	AUAUUUAUU	AAGCACUU
	5158	AAAGUGCU	CUGAUGA	X	GAA	AAUAAAUA	UAUUUAUUA	AGCACUUU
	5165	GGAGCAUA	CUGAUGA	X	GAA	AGUGCUUA	UAAGCACUU	UAUGCUCC
5	5166	AGGAGCAU	CUGAUGA	X	GAA	AAGUGCUU	AAGCACUUU	AUGCUCCU
	5167	AAGGAGCA	CUGAUGA	X	GAA	AAAGUGCU	AGCACUUUA	UGCUCCUU
	5172	GUGCCAAG	CUGAUGA	X	GAA	AGCAUAAA	UUUAUGCUC	CUUGGCAC
	5175	GCUGUGCC	CUGAUGA	X	GAA	AGGAGCAU	AUGCUCCUU	GGCACAGC
	519 5	GCAUAAAU	CUGAUGA	X	GAA	ACACAUCA	UGAUGUGUA	AUUUAUGC
10	5198	CUUGCAUA	CUGAUGA	X	GAA	AUUACACA	UGUGUAAUU	UAUGCAAG
	5199	GCUUGCAU	CUGAUGA	X	GAA	AAUUACAC	GUGUAAUUU	AUGCAAGC
	5200	AGCUUGCA	CUGAUGA	X	GAA	AAAUUACA	UGUAAUUUA	UGCAAGCU
	5209	UGGAGAGG	CUGAUGA	X	GAA	AGCUUGCA	UGCAAGCUC	CCUCUCCA
	5213	UAGCUGGA	CUGAUGA	X	GAA	AGGGAGCU	AGCUCCCUC	UCCAGCUA
15	5215	CCUAGCUG	CUGAUGA	X	GAA	AGAGGGAG	CUCCCUCUC	CAGCUAGG
	5221	CUGAGUCC	CUGAUGA	X	GAA	AGCUGGAG	CUCCAGCUA	GGACUCAG
	5227	AAUAUCCU	CUGAUGA	X	GAA	AGUCCUAG	CUAGGACUC	AGGAUAUU
	5233	UUGACUAA	CUGAUGA	X	GAA	AUCCUGAG	CUCAGGAUA	UUAGUCAA
	5235	CAUUGACU	CUGAUGA	X	GAA	AUAUCCUG	CAGGAUAUU	AGUCAAUG
20	5236	UCAUUGAC	CUGAUGA	X	GAA	AAUAUCCU	AGGAUAUUA	GUCAAUGA
	5239	GGCUCAUU	CUGAUGA	X	GAA	ACUAAUAU	AUAUUAGUC	AAUGAGCC
	5250	υυςςυυυυ	CUGAUGA	X	GAA	AUGGCUCA	UGAGCCAUC	AAAAGGAA
	5273	AAAUAAGA	CUGAUGA	X	GAA	AGGUUUUU	AAAAACCUA	UCUUAUUU
	5275	GAAAAUAA	CUGAUGA	X	GAA	AUAGGUUU	AAACCUAUC	UUAUUUUC
25	5277	AUGAAAAU	CUGAUGA	X	GAA	AGAUAGGU	ACCUAUCUU	AUUUUCAU
	5278	GAUGAAAA	CUGAUGA	X	GAA	AAGAUAGG	CCUAUCUUA	UUUUCAUC
	5280	CAGAUGAA	CUGAUGA	X	GAA	AUAAGAUA	UAUCUUAUU	UUCAUCUG
	5281	ACAGAUGA	CUGAUGA	X	GAA	AAUAAGAU	AUCUUAUUU	UCAUCUGU
	5282	AACAGAUG	CUGAUGA	X	GAA	AAAUAAGA	UCUUAUUUU	CAUCUGUU
30	5283	AAACAGAU	CUGAUGA	X	GAA	AAAAUAAG	CUUAUUUUC	AUCUGUUU
	5286	AUGAAACA	CUGAUGA	X	GAA	AUGAAAAU	AUUUUCAUC	UGUUUCAU
	5290	AGGUAUGA	CUGAUGA	X	GAA	ACAGAUGA	UCAUCUGUU	UCAUACCU
	5291	AAGGUAUG	CUGAUGA	X	GAA	AACAGAUG	CAUCUGUUU	CAUACCUU

	5292	CAAGGUAU	CUGAUGA	X	GAA	AAACAGAU	AUCUGUUUC	AUACCUUG
	5295	AGACAAGG	CUGAUGA	X	GAA	AUGAAACA	UGUUUCAUA	CCUUGUCU
	5299	CCCCAGAC	CUGAUGA	X	GAA	AGGUAUGA	UCAUACCUU	GUCUGGGG
	5302	AGACCCCA	CUGAUGA	X	GAA	ACAAGGUA	UACCUUGUC	UGGGGUCU
5	5309	CGUCAUUA	CUGAUGA	X	GAA	ACCCCAGA	UCUGGGGUC	UAAUGACG
	5311	AUCGUCAU	CUGAUGA	X	GAA	AGACCCCA	UGGGGUCUA	AUGACGAU
	5331	CCCAUGUC	CUGAUGA	X	GAA	ACCCUGUU	AACAGGGUA	GACAUGGG
	5350	cccuuuuc	CUGAUGA	X	GAA	ACCCUGUC	GACAGGGUA	GAAAAGGG
	5367	.ACCCCAAA	CUGAUGA	X	GAA	AGCGGGCA	UGCCCGCUC	UUUGGGGU
10	5369	AGACCCCA	CUGAUGA	X	GAA	AGAGCGGG	CCCGCUCUU	UGGGGUCU
	5370	UAGACCCC	CUGAUGA	X	GAA	AAGAGCGG	CCGCUCUUU	GGGGUCUA
	53 76	CAUCUCUA	CUGAUGA	X	GAA	ACCCCAAA	UUUGGGGUC	UAGAGAUG
	5378	CUCAUCUC	CUGAUGA	X	GAA	AGACCCCA	UGGGGUCUA	GAGAUGAG
	539 5	AUUUUAGA	CUGAUGA	X	GAA	ACCCAGGG	CCCUGGGUC	UCUAAAAU
15	53 97	CCAUUUUA	CUGAUGA	X	GAA	AGACCCAG	CUGGGUCUC	UAAAAUGG
	5399	AGCCAUUU	CUGAUGA	X	GAA	AGAGACCC	GGGUCUCUA	AAAUGGCU
	5408	UUCUAAGA	CUGAUGA	X	GAA	AGCCAUUU	AAAUGGCUC	UCUUAGAA
	5410	ACUUCUAA	CUGAUGA	X	GAA	AGAGCCAU	AUGGCUCUC	UUAGAAGU
	5412	CAACUUCU	CUGAUGA	X	GAA	AGAGAGCC	GGCUCUCUU	AGAAGUUG
20	5413	ACAACUUC	CUGAUGA	Х	GAA	AAGAGAGC	GCUCUCUUA	GAAGUUGU
	5419	GCACAUAC	CUGAUGA	X	GAA	ACUUCUAA	UUAGAAGUU	GUAUGUGC
	5422	UUUGCACA	CUGAUGA	X	GAA	ACAACUUC	GAAGUUGUA	UGUGCAAA
	5432	CAGACCAU	CUGAUGA	X	GAA	AUUUGCAC	GUGCAAAUU	AUGGUCUG
	5433	ACAGACCA	CUGAUGA	X	GAA	AAUUUGCA	UGCAAAUUA	UGGUCUGU
25	5438	AGCACACA	CUGAUGA	X	GAA	ACCAUAAU	AUUAUGGUC	UGUGUGCU
	5447	CACGACCU	CUGAUGA	X	GAA	AGCACACA	UGUGUGCUU	AGGUCGUG
	5448	GCACGACC	CUGAUGA	X	GAA	AAGCACAC	GUGUGCUUA	GGUCGUGC
	5452	GUGUGCAC	CUGAUGA	X	GAA	ACCUAAGC	GCUUAGGUC	GUGCACAC
	5475	CCAGCUGU	CUGAUGA	X	GAA	ACCGGCUC	GAGCCGGUC	ACAGCUGG
30	5497	AAAGCAGC	CUGAUGA	X	GAA	AUUCAUCG	CGAUGAAUA	GCUGCUUU
	5504	CUCUCCCA	CUGAUGA	x	GAA	AGCAGCUA	UAGCUGCUU	UGGGAGAG
	5505	GCUCUCCC	CUGAUGA	x	GAA	AAGCAGCU	AGCUGCUUU	GGGAGAGC
	5524	UAAGUGGC	CUGAUGA	X	GAA	AGCAUGCU	AGCAUGCUA	GCCACUUA

	5531	AGAGAAUU	CUGAUGA	X	GAA	AGUGGCUA	UAGCCACUU	AAUUCUCU
	5532	CAGAGAAU	CUGAUGA	X	GAA	AAGUGGCU	AGCCACUUA	AUUCUCUG
	5535	GGUCAGAG	CUGAUGA	X	GAA	AUUAAGUG	CACUUAAUU	CUCUGACC
	5536	CGGUCAGA	CUGAUGA	X	GAA	AAUUAAGU	ACUUAAUUC	UCUGACCG
5	5538	CCCGGUCA	CUGAUGA	X	GAA	AGAAUUAA	UUAAUUCUC	UGACCGGG
	5554	GUACCCAU	CUGAUGA	X	GAA	AUGCUGGC	GCCAGCAUC	AUGGGUAC
	5561	GGAGCAGG	CUGAUGA	x	GAA	ACCCAUGA	UCAUGGGUA	CCUGCUCC
	5568	ACACAGGG	CUGAUGA	X	GAA	AGCAGGUA	UACCUGCUC	CCCUGUGU
	5577	GGAUGGGG	CUGAUGA	X	GAA	ACACAGGG	CCCUGUGUA	CCCCAUCC
10	5584	ACCUUAAG	CUGAUGA	X	GAA	AUGGGGUA	UACCCCAUC	CUUAAGGU
	5587	AAAACCUU	CUGAUGA	X	GAA	AGGAUGGG	CCCAUCCUU	AAGGUUUU
	5588	GAAAACCU	CUGAUGA	X	GAA	AAGGAUGG	CCAUCCUUA	AGGUUUUC
	5593	AGACAGAA	CUGAUGA	X	GAA	ACCUUAAG	CUUAAGGUU	UUCUG UC U
	5594	CAGACAGA	CUGAUGA	X	GAA	AACCUUAA	UUAAGGUUU	UCUGUCUG
15	5595	UCAGACAG	CUGAUGA	X	GAA	AAACCUUA	UAAGGUUUU	CUGUCUGA
	5596	AUCAGACA	CUGAUGA	X	GAA	AAAACCUU	AAGGUUUUC	UGUCUGAU
	5600	UCUCAUCA	CUGAUGA	X	GAA	ACAGAAAA	UUUUCUGUC	UGAUGAGA
	5627	UCAGUGGG	CUGAUGA	X	GAA	AUUGCACU	AGUGCAAUC	CCCACUGA
	5660	UGCACCAA	CUGAUGA	X	GAA	AGCCACAG	CUGUGGCUC	UUGGUGCA
20	5662	AGUGCACC	CUGAUGA	X	GAA	AGAGCCAC	GUGGCUCUU	GGUGCACU
	5671	UGGCUGGU	CUGAUGA	X	GAA	AGUGCACC	GGUGCACUC	ACCAGCCA
	5685	UACUUGUC	CUGAUGA	X	GAA	AGUCCUGG	CCAGGACUA	GACAAGUA
	5693	cccuuucc	CUGAUGA	X	GAA	ACUUGUCU	AGACAAGUA	GGAAAGGG
	5704	GUGGCUAG	CUGAUGA	X	GAA	AGCCCUUU	AAAGGGCUU	CUAGCCAC
25	5705	UGUGGCUA	CUGAUGA	X	GAA	AAGCCCUU	AAGGGCUUC	UAGCCACA
	5707	AGUGUGGC	CUGAUGA	X	GAA	AGAAGCCC	GGGCUUCUA	GCCACACU
	5731	CCCUACCU	CUGAUGA	X	GAA	AUUUUCUU	AAGAAAAUC	AGGUAGGG
	5736	GCCAGCCC	CUGAUGA	X	GAA	ACCUGAUU	AAUCAGGUA	GGGCUGGC
	5754	UGGACAAA	CUGAUGA	X	GAA	AUGUCUUU	AAAGACAUC	UUUGUCCA
30	5756	AAUGGACA	CUGAUGA	X	GAA	AGAUGUCU	AGACAUCUU	UGUCCAUU
	5757	GAAUGGAC	CUGAUGA	X	GAA	AAGAUGUC	GACAUCUUU	GUCCAUUC
	5760	UGCGAAUG	CUGAUGA	X	GAA	ACAAAGAU	AUCUUUGUC	CAUUCGCA
	5764	CUUUUGCG	CUGAUGA	X	GAA	AUGGACAA	UUGUCCAUU	CGCAAAAG

	5765	GCUUUUGC	CUGAUGA	X	GAA	AAUGGACA	UGUCCAUUC	GCAAAAGC
	577 5	GCCGACAA	CUGAUGA	X	GAA	AGCUUUUG	CAAAAGCUC	UUGUCGGC
	5777	CAGCCGAC	CUGAUGA	X	GAA	AGAGCUUU	AAAGCUCUU	GUCGGCUG
	5780	CUGCAGCC	CUGAUGA	X	GAA	ACAAGAGC	GCUCUUGUC	GGCUGCAG
5	5794	GCCUGACU	CUGAUGA	X	GAA	ACACACUG	CAGUGUGUA	AGUCAGGC
	5798	CAUCGCCU	CUGAUGA	X	GAA	ACUUACAC	GUGUAAGUC	AGGCGAUG
	5818	UUCUCUGG	CUGAUGA	X	GAA	AGCCUCUG	CAGAGGCUA	CCAGAGAA
	5852	GGAUGAGA	CUGAUGA	X	GAA	ACCUCAGG	CCUGAGGUU	UCUCAUCC
	5853	UGGAUGAG	CUGAUGA	X	GAA	AACCUCAG	CUGAGGUUU	CUCAUCCA
10	5854	CUGGAUGA	CUGAUGA	X	GAA	AAACCUCA	UGAGGUUUC	UCAUCCAG
	5856	AUCUGGAU	CUGAUGA	X	GAA	AGAAACCU	AGGUUUCUC	AUCCAGAU
	5859	GAUAUCUG	CUGAUGA	X	GAA	AUGAGAAA	UUUCUCAUC	CAGAUAUC
	5865	UUGCUGGA	CUGAUGA	X	GAA	AUCUGGAU	AUCCAGAUA	UCCAGCAA
	5867	AAUUGCUG	CUGAUGA	X	GAA	AUAUCUGG	CCAGAUAUC	CAGCAAUU
15	587 5	CACCCCCC	CUGAUGA	X	GAA	AUUGCUGG	CCAGCAAUU	GGGGGGUG
	5896	GGACCAUC	CUGAUGA	X	GAA	AUGGUCUU	AAGACCAUA	GAUGGUCC
	5903	UAAUACAG	CUGAUGA	X	GAA	ACCAUCUA	UAGAUGGUC	CUGUAUUA
	5908	CGGAAUAA	CUGAUGA	X	GAA	ACAGGACC	GGUCCUGUA	UUAUUCCG
	5910	AUCGGAAU	CUGAUGA	X	GAA	AUACAGGA	UCCUGUAUU	AUUCCGAU
20	5911	AAUCGGAA	CUGAUGA	X	GAA	AAUACAGG	CCUGUAUUA	UUCCGAUU
	591 3	AAAAUCGG	CUGAUGA	X	GAA	AUAAUACA	UGUAUUAUU	CCGAUUUU
	5914	UAAAAUCG	CUGAUGA	X	GAA	AAUAAUAC	GUAUUAUUC	CGAUUUUA
	5919	AAUUAUUAA					AUUCCGAUU	UAAUAAUU
	5920	GAUUAUUA	CUGAUGA	X	GAA	AAUCGGAA	UUCCGAUUU	UAAUAAUC
25	5921						UCCGAUUUU	
	5922	UAGAUUAU	CUGAUGA	X	GAA	AAAAUCGG	CCGAUUUUA	AUAAUCUA
	5 9 25	AAUUAGAU	CUGAUGA	X	GAA	AUUAAAAU	AUAAUUUUA	AUCUAAUU
	592 8	ACGAAUUA	CUGAUGA	X	GAA	AUUAUUAA	UUAAUAAUC	UAAUUCGU
	59 30	UCACGAAU	CUGAUGA	X	GAA	AGAUUAUU	AAUAAUCUA	AUUCGUGA
30	593 3	UGAUCACG	CUGAUGA	X	GAA	AUUAGAUU	AAUCUAAUU	CGUGAUCA
	5934						AUCUAAUUC	
	5940	CUCUUAAU	CUGAUGA	X	GAA	AUCACGAA	UUCGUGAUC	AUUAAGAG
	5943	AGUCUCUU	CUGAUGA	X	GAA	AUGAUCAC	GUGAUCAUU	AAGAGACU

	5944	AAGUCUCU	CUGAUGA	X	GAA	AAUGAUCA	UGAUCAUUA	AGAGACUU
	5952	AUUUACUA	CUGAUGA	X	GAA	AGUCUCUU	AAGAGACUU	UAGUAAAU
	5953	CAUUUACU	CUGAUGA	X	GAA	AAGUCUCU	AGAGACUUU	AGUAAAUG
	5954	ACAUUUAC	CUGAUGA	X	GAA	AAAGUCUC	GAGACUUUA	GUAAAUGU
5	5957	GGGACAUU	CUGAUGA	X	GAA	ACUAAAGU	ACUUUAGUA	AAUGUCCC
	5963	GGAAAAGG	CUGAUGA	X	GAA	ACAUUUAC	GUAAAUGUC	CCUUUUCC
	5967	UGUGGGAA	CUGAUGA	X	GAA	AGGGACAU	AUGUCCCUU	UUCCCACA
	5968	UUGUGGGA	CUGAUGA	X	GAA	AAGGGACA	UGUCCCUUU	UCCCACAA
	5969	UUUGUGGG	CUGAUGA	X	GAA	AAAGGGAC	GUCCCUUUU	CCCACAAA
10	5970	UUUUGUGG	CUGAUGA	X	GAA	AAAAGGGA	ucccuuuuc	CCACAAAA
	5981	CUUUUCUU	CUGAUGA	X	GAA	ACUUUUGU	ACAAAAGUA	AAGAAAAG
	5992	AAUCCCGA	CUGAUGA	X	GAA	AGCUUUUC	GAAAAGCUA	UCGGGAUU
	5994	AGAAUCCC	CUGAUGA	X	GAA	AUAGCUUU	AAAGCUAUC	GGGAUUCU
	6000	AACCAGAG	CUGAUGA	X	GAA	AUCCCGAU	AUCGGGAUU	CUCUGGUU
15	6001	GAACCAGA	CUGAUGA	X	GAA	AAUCCCGA	UCGGGAUUC	UCUGGUUC
	60 03	CAGAACCA	CUGAUGA	X	GAA	AGAAUCCC	GGGAUUCUC	UGGUUCUG
	6008	UUAAGCAG	CUGAUGA	X	GAA	ACCAGAGA	UCUCUGGUU	CUGCUUAA
	6009	UUUAAGCA	CUGAUGA	X	GAA	AACCAGAG	CUCUGGUUC	UGCUUAAA
	6014	AAGUCUUU	CUGAUGA	X	GAA	AGCAGAAC	GUUCUGCUU	AAAGACUU
20	6015	UAAGUCUU	CUGAUGA	X	GAA	AAGCAGAA	UUCUGCUUA	AAGACUUA
	6022	CCAAAGCU	CUGAUGA	X	GAA	AGUCUUUA	UAAAGACUU	AGCUUUGG
	6023	UCCAAAGC	CUGAUGA	X	GAA	AAGUCUUU	AAAGACUUA	GCUUUGGA
	6027	AGGCUCCA	CUGAUGA	X	GAA	AGCUAAGU	ACUUAGCUU	UGGAGCCU
	6028	UAGGCUCC	CUGAUGA	X	GAA	AAGCUAAG	CUUAGCUUU	GGAGCCUA
25	6036	AACUUUCA	CUGAUGA	X	GAA	AGGCUCCA	UGGAGCCUA	UGAAAGUU
	6044	GGCUGAUC	CUGAUGA	x	GAA	ACUUUCAU	AUGAAAGUU	GAUCAGCC

Where "X" represents stem II region of a HH ribozyme (Hertel et al., 1992 Nucleic Acids Res. 20 3252). The length of stem II may be \geq 2 base-pairs.

18

Table IX: Mouse flt1 VEGF Receptor-Hairpin Ribozyme and Substrate Sequence

						1	84									
Substrate		AUGGUCA GCU GCUGGGAC	GUCAGCU GCU GGGACACC	CACCGCG GUC UUGCCUUA	ACGCGCU GCU CGGGUGUC	GGUGUCU GCU UCUCACAG	CAGGCCA GAC UCUCUUUC	GGAGGCA GCC CACUCAUG	GGUCUCU GCC CACGACCG	CCCAUCG GCC UGUGGGAG	GAAGACA GCU CAUCAUCC	AUCCCCU GCC GGGUGACG	UACCCCU GAU GGGCAAAG	UAGGACU GCU GAACUGCG	ACUAUCU GAC CCAUCGGC	AUCGGCA GAC CAAUACAA
HP Ribozyme Sequence		GUCCCAGC AGAA GACCAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GGUGUCCC AGAA GCUGAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UAAGGCAA AGAA GCGGUG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GACACCCG AGAA GCGCGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CUGUGAGA AGAA GACACC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GAAAGAGA AGAA GGCCUG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CAUGAGUG AGAA GCCUCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CGGUCGUG AGAA GAGACC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CUCCCACA AGAA GAUGGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GGAUGAUG AGAA GUCUUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CGUCACCC AGAA GGGGAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CUUUGCCC AGAA GGGGUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	CGCAGUUC AGAA GUCCUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	GCCGAUGG AGAA GAUAGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA	UUGUAUUG AGAA GCCGAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA
nt.	tion	33	36	20	67	79	166	197	214	266	487	501	566	640	691	703
		Ŋ					10					5				

PCT/US96/17480

185

GUGCCGAA UACGCCC GCC GAGCCCAG UUUCAACA GGUGCAGG GCU GGGCAGCA CCCUGGAA CCACGGGC UCUUGUCC GGCAGCG GAU UGACCGGA GCGUGAAG CUAUCGGC GUCCAUGA CAUGAAAG CGCUAUUU GAU CUACGAAA GAC UCUCAGAC ರಿದಿರಿದಿರುವ GGGCCUUC GCC GAAGGAGA GCU GCU UGAGACU GCU ggg GUC GCO GAU GAC GNC CGUUCCA GUC GUC ACUCUCA GAC UACAGCU GCC GGAAGCA GAAGACG AUCGGCU GAAGUCU GGUGGCU GAUGCCA ACGGGCA UACACCU CCUAUCG AACCUCA UCUAUCC UGUCACA AUCUACA CUGGGCUC AGAA GGCGUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCUGCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGUGUA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGAACG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCUUCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GAUAGG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA GACUUC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUCUCA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GCCCGU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUCUUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCCGAU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GAGGUU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GAUAGA ACCAGAGAAACACGCGUGGUGGUACAUUACCUGGUA GCCACC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GAGAGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUAGAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCUGUA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUGACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGCAUC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA UCCGGUCA AGAA AGAA GCCGAUAG AGAA UUUCGUAG AGAA UCUCCUUC AGAA GCCCGUGG AGAA CUUCACGC AGAA UGUUGAAA AGAA AGAA CUUUCAUG AGAA GGCCCGGC AGAA SAAGGCCC AGAA GGACAAGA AGAA AGAA AGAA GUCUGAGA AGAA UUCCAGGG AGAA UUCGGCAC AGAA UCAUGGAC CCUGCACC AAAUAGCG necneccc 1090 1093 1169 1315 1612 1629 1051 1081 1363 1604 1632 1688 1730 736 988 754 992 960 871 10 S 15

186

CCACACAG AGAA GUUUCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

1753

S

UGAAACU GUC CUGUGUGG

10

GAUGUGAG

AAGCUCU GAU

GAGCUU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA

GAUAGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

UAGUGUCC AGAA

3754

3772

CUCACAUC AGAA

3650

GGGAGCCC AGAA GAGUGC ACCAGAGAAACACACGUUGUGGGAACAUUACCUGGUA

GGACACUA

GCU

ACUAUCA

CCCCCCC

GCACUCU GCU

187

GUU UCCAAGUG GAACCCU GAU UAUGUGAG GCCUGAAG GCAUGCG GAU GAGAACCC GUGACCU GCU UCAAGCCA UAGAAACA GCU UUGCAGAU GUCAGCA GCU CAAGUGUC GUCACCA GCU CCAGCUUC GCU UCCCUGAA CCUCACCA UUCCUACA CUCCAGAA UGAAGGAA GUU UGCUGAAC CCACAUUU GAU GAC gcc GAU AGUUUCU GUC GCC CCAAGCA GCC AAGGACG CCAUACU AGCUCCA AAGACCU UCCUACA UUCUGCA UGCAGCC 9222299 CUUUGCA UGGCUUGA AGAA GGUCAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA AUCUGCAA AGAA GUCCUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGUGAC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGAGCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCUUGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UGUAGGAA AGAA GGUCUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUAGGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAAACU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGUUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CUUCAGGC AGAA GCAGAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCUGCA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA SEGUUCUC AGAA GCAUGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUUCAGCA AGAA GGGGCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA GCUGAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUAUGG GCAAAG UUCUGGAG AGAA CUCACAUA AGAA AGAA AGAA GACACUUG AGAA UGGUGAGG AGAA CACUUGGA AGAA UUCCUUCA AGAA AGAA AGAA UGUUUCUA AAAUGUGG GAAGCUGG UUCAGGGA 3496 3615 3179 3360 3379 3623 2913 2928 3022 3033 3064 3357 3463 3553 2934 3001 15 10 വ

GCCAGCU GCU UUUCGUGA

UGUUGCU GUU UUGACUAA

CGCCCACC

ggg

GGCGACC

GUCGCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA

GGCGGU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA

GGCCGGUG AGAA

4294

GCAACA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

UVAGUCAA AGAA

4168

4113

GGGGGG AGAA

4290

UCACGAAA AGAA GCUGGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA

CACCGGCC

SCC

ACCGCCC

188 CUGCCGAG UGAAGCG GUU CACCUGGA GAGGCCCA AGGCCCA GCU UCUGCUUC GCU UCUCCAGC UUCUCCA GCU GUGGCCAC GAGUCCU GCU GUUCUCCA UCCUGCU GUU CUCCACCC ACCCCCA GAC UACAACUC CGCCUAAA GCC CCGACAAC ACAACCA GCC CCUGACAG CUAUUCC GCU CCACAGGA GGAGCCA GCU GCUUUUCG CCCGCCC GCC UAAAGCUU ACUUUCC GAU gcc ccaccc ecc CCGAUCU AGCUUCU CUCACCA UCCAGGUG AGAA GCUUCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAAAGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAUCGG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGGCCU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GCUGGAGA AGAA GAAGCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGAGAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UGGAGAAC AGAA GGACUC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGUGGAG AGAA GCAGGA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAGUUGUA AGAA GGGGGU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGGAGG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA AAGCUUUA AGAA GGCGGG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUUGUCGG AGAA GGUGAG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA AGAA GGUUGU ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA UCCUGUGG AGAA GAAUAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGCUCC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CUCGGCAG AGAA UGGGCCUC AGAA AGAA AGAA UUUAGGCG AGAA CGAAAAGC AGAA GAAGCAGA GUGGCCAC CUGUCAGG 3796 3886 3903 3969 3881 3897 3912 3972 3986 4018 4022 4040 4095 4110 4053 ហ 10 15

PCT/US96/17480

CUUUGGGG

gcn

GGUGCCC

GGCACC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA

CCCCAAAG AGAA

5363

189

UGGUCCA GUU UGGCCUAG GGGCUCAA UNAUAUAU UGAGAGGA CAUAUUUA UCAUACCU UCUCUUAU CUGUGGAG GUUUCGGG nceeeccc GUCUGUUU GUUGUCU GUU UACCAUCC CCUCUAGU CUUCGCAU CACGGGGA GCU GUGGGACU CUGCUCUG CUGUCUCU GM GM GCU GUC GCU GUU GNN gcn GAU GNC GUU AUGCACU GAC cuacucu auc CAGGCCU GAC ದಿದ್ದ CUCCGCU GUCUUCU UVAUCCU GCAUACU UUCAUCU AUCAUCA GCCUACU CAAGGCA CUGACCU CCCUGCA UGCGUCC GGCCNCC AGUAUCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAUGAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCAGGG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GUGCAU ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA GAGCAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GACGCA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GAGGCC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCGGAG ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GAAGAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GACAAC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAUGAU ACCAGAGAAACACGCUGUGGGGGACAUUACCUGGUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GUAUGC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CUAGGCCA AGAA GGACCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GGAUAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GAUACU ACCAGAGAAACACGCUGUGGGGACAUUACCUGGUA CCCCOC GCCNNG GGUCAG GUAGGC AGAA AGAA AGAA AGUCCCAC AGAA AGAA GGGCCCGA AGAA GGAUGGUA AGAA AUGCGAAG AGAA AGAA UCCUCUCA AGAA UNAAUAUG AGAA AGGUAUGA AGAA CUCCACAG AGAA AGAA CAGAGCAG AGAA AGAA AUAAGAGA AGAA AGAGACAG CCCGAAAC AAACAGAC ACUAGAGG nccccene AUAUAUAA UUGAGCCC 4525 4528 4785 4809 4912 5119 4329 4643 4834 5144 5287 4378 4383 4388 4457 4650 4724 4771 10 ហ 15

190

CACACCU GCC GGAGCCGG GGGCAGAC GAUGAAUA AAUAGCU GCU UUGGGAGA AUUCUCU GAC CGGGCCAG GGUACCU GCU CCCCUGUG GUUUUCU GUC UGAUGAGA UCUGUCU GAU GAGACUGG GCCUGCA GCC CACUGUGG CUUGUCG GCU GCAGUGUG AGAAACG GAU GAGAACAG UGCAGCCC UNAUUCC GAU UUUAAUAA AACAGCA GCC UGAGGUUU UGGUUCU GCU UAAAGACU GGUCACA GCU GAC UGAGACA GCC CUGGGCA CCGGCUCC AGAA GGUGUG ACCAGAGAAACACACGUUGUGGGAACAUUACCUGGUA GUCUGCCC AGAA GUGACC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UAUUCAUC AGAA GCCCAG ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UCUCCCAA AGAA GCUAUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CUGGCCCG AGAA GAGAAU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CACAGGGG AGAA GGUACC ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UCUCAUCA AGAA GAAAAC ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA GACAGA ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA GGGCUGCA AGAA GUCUCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA GCAGGC ACCAGAGAACACACGUUGUGGUACAUUACCUGGUA CACACUGC AGAA GACAAG ACCAGAGAAACACGUUGUGGUACAUUACCUGGUA CUGUUCUC AGAA GUUUCU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AAACCUCA AGAA GCUGUU ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA UUAUUAAA AGAA GAAUAA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA AGUCUJUA AGAA GAACCA ACCAGAGAAACACACGUUGUGGUACAUUACCUGGUA CCAGUCUC AGAA CCACAGUG AGAA 5462 5478 5486 5500 5539 5639 5564 5597 5601 5646 5781 5829 5842 5915 6010 ഗ 10 15

191

<u>Table X: Homologous Hammerhead Ribozyme Target Sites</u>

<u>Between Human flt-1 and KDR RNA</u>

	nt.	flt-1	nt.	KDR
	Posi-	Target Sequence	Posi-	Target Sequence
5	tion		tion	
	3388	CCGGGAU A UUUAUAA	3151	CCGGGAU A UUUAUAA
	2174	AAUGUAU A CACAGGG	3069	Aguguau c CACAGGG
	2990	UGCAAAU A UGGAAAU	2756	UGCAAAU u UGGAAAc
	2693	CUCCCUU A UGAUGCC	2459	CUGCCUU A UGAUGCC
10	2981	GUUGAAU A CUGCAAA	2747	GUgGAAU u CUGCAAA
	1359	UAUGGUU A AAAGAUG	2097	UgUGGUU u AAAGAUa
	3390	GGGAUAU U UAUAAGA	3153	GGGAUAU U UAUAAag
	3391	GGAUAUU U AUAAGAA	3154	GGAUAUU U AUAAagA
	2925	ACGUGGU U AACCUGC	2691	Auguggu c AACCUuC
15	7140	UAUUUCU A GUCAUGA	2340	UACUUCU u GUCAUCA
	1785	CAAUAAU A GAAGGAA	1515	CucUAAU u GAAGGAA
	2731	GAGACUU A AACUGGG	768	uuGACUU c AACUGGG
	3974	GAUGACU A CCAGGGC	1466	GAgGACU u CCAGGGa
	6590	UUAAUGU A GAAAGAA	2603	aaAAUGU u GAAAGAA
20	6705	GCCAUUU A UGACAAA	3227	aCaAUUU u UGACAgA
	974	GUCAAAU U ACUUAGA	147	uUCAAAU U ACUUgcA
	1872	AUAAAGU U GGGACUG	1602	AcAAAGU c GGGAgaG
	2333	ACUUGGU U UAAAAAC	1088	AaaUGGU a UAAAAAu
	2775	AAGUGGU U CAAGCAU	1745	AcaUGGU a CAAGCuU
25	3533	UUCUCCU U AGGUGGG	3296	UUuUCCU U AGGUGcu
	3534	UCUCCUU A GGUGGGU	3297	UuUCCUU A GGUGcuU
	3625	GUACUCU A CUCCUGA	4054	GagCUCU c CUCCUGu
	1814	AGCACCU U GGUUGUG	1059	AGuACCU U GGUUacc
	2744	GGCAAAU C ACUUGGA	147	uuCAAAU u ACUUGcA
30	2783	CAAGCAU C AGCAUUU	796	gAAGCAU C AGCAUaa

192

	3613	GAGAGCU	С	CUGAGUA	2968	GgaAGCU	С	CUGAagA
	4052	AAGGCCU	С	GCUCAAG	1923	ucuGCCU	u	GCUCAAG
	5305	UCUCCAU	A	UCAAAAC	456	ggUCCAU	u	UCAAAuC
	7158	AUGUAUU	U	UGUAUAC	631	gucuauu	a	UGUAcAu
5	1836	CUAGAAU	U	UCUGGAA	1007	aUgGAAU	С	UCUGGug
	2565	cucucuu	С	UGGCUCC	2328	uguUCUU	С	UGGCUaC
	4250	CUGUACU	С	CACCCCA	3388	uUaUACU	a	CACCagA
	7124	ACAUGGU	U	UGGUCCU	3778	cagUGGU	a	UGGUuCU
	436	AUGGUCU	U	UGCCUGA	1337	AcGGUCU	a	UGCCauu
10	2234	GCACCAU	A	CCUCCUG	1344	augCCAU	u	CCUCCcc
	2763	GGGCUUU	U	GGAAAAG	990	uuGCUUU	U	GGAAguG
	4229	CCAGACU	A	CAACUCG	767	auuGACU	u	CAACUgG
	5301	GUUUUCU	С	CAUAUCA	3307	ugcUUCU	С	CAUAUCc
	6015	AGAAUGU	A	UGCCUCU	1917	AcuAUGU	С	UGCCUug
15	6095	AUUCCCU	A	GUGAGCC	1438	AUaCCCU	u	GUGAaga
	6236	UGUUGUU	С	CUCUUCU	76	UagUGUU	u	CUCUUga
	5962	GCUUCCU	U	UUAUCCA	3099	auaUCCU	С	UUAUCgg
	7629	UAUAUAU	U	CUCUGCU	3096	gAaAUAU	С	CUCUuaU

Lowercase letters are used to represent sequence variance 20 between flt-1 and KDR RNA

193

Table XI: 2.5 μmol RNA Synthesis Cycle

	Reagent	Equivalents	Amount	Wait Time*
	Phosphoramidites	6.5	$163 \mu L$	2.5
	S-Ethyl Tetrazole	23.8	238μL	2.5
5	Acetic Anhydride	100	233 μL	5 sec
	N-Methyl Imidazole	186	233 μL	5 sec
	TCA	83.2	1.73 mL	21 sec
	Iodine	8.0	1.18 mL	45 sec
	Acetonitrile	NA	6.67 ml	NA

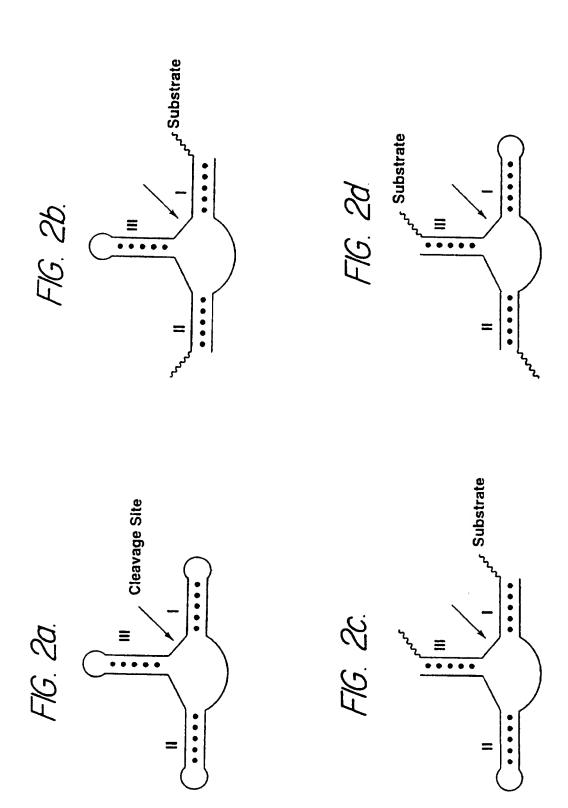
Claims

- Nucleic acid molecule which modulates the synthesis, expression and/or stability of an mRNA encoding one or more receptors of vascular endothelial growth
 factor.
 - 2. The nucleic acid of claim 1, wherein said receptor is flt-1, KDR and/or flk-1.
 - 3. The nucleic acid of claim 1 or 2, wherein said molecule is an enzymatic nucleic acid molecule.
- 4. The nucleic acid molecule of claim 3, wherein, the binding arms of said enzymatic nucleic acid contain sequences complementary to the substrate nucleotide base sequences in any one of Tables II to IX.
- The nucleic acid molecule of claims 3 or 4,
 wherein said nucleic acid molecule is in a hammerhead motif.
- 6. The enzymatic nucleic acid molecule of claim 3 or 4, wherein said nucleic acid molecule is in a hairpin, hepatitis Delta virus, group I intron, VS nucleic acid or 20 RNaseP nucleic acid motif.
 - 7. The enzymatic nucleic acid molecule of any of claims 3 or 4, wherein said ribozyme comprises between 12 and 100 bases complementary to the RNA of said region.
- 8. The enzymatic nucleic acid of claim 7, wherein 25 said ribozyme comprises between 14 and 24 bases complementary to the RNA of said region.
 - 9. Enzymatic nucleic acid molecule consisting essentially of any ribozyme sequence selected from those shown in Tables II to IX.

- 10. A mammalian cell including a nucleic acid molecule of any of claims 1, 2 or 3.
- 11. The cell of claim 10, wherein said cell is a human cell.
- 12. An expression vector comprising nucleic acid encoding the nucleic acid molecule of any of claims 1, 2, 3 or 4, in a manner which allows expression and/or delivery of that RNA molecule within a mammalian cell.
- 13. The expression vector of claim 12, wherein said 10 nucleic acid is an enzymatic nucleic acid.
 - 14. A mammalian cell including an expression vector of any of claims 12 or 13.
 - 15. The cell of claim 14, wherein said cell is a human cell.
- 16. A method for treatment of a patient having a condition associated with the level of flt-1, KDR and/or flk-1, wherein the patient, tissue donor or population of corresponding cells is administered a therapeutically effective amount of an enzymatic nucleic acid molecule of claims 1, 2, 3 or 4.
 - 17. A method for treatment of a condition related to the level of flt-1, KDR and/or flk-1 activity by administering to a patient an expression vector of claim 12.
- 18. The method of claims 16 or 17, wherein said 25 patient is a human.
 - 19. The nucleic acid of claim 1 or 2, wherein said molecule is an antisense nucleic acid molecule.

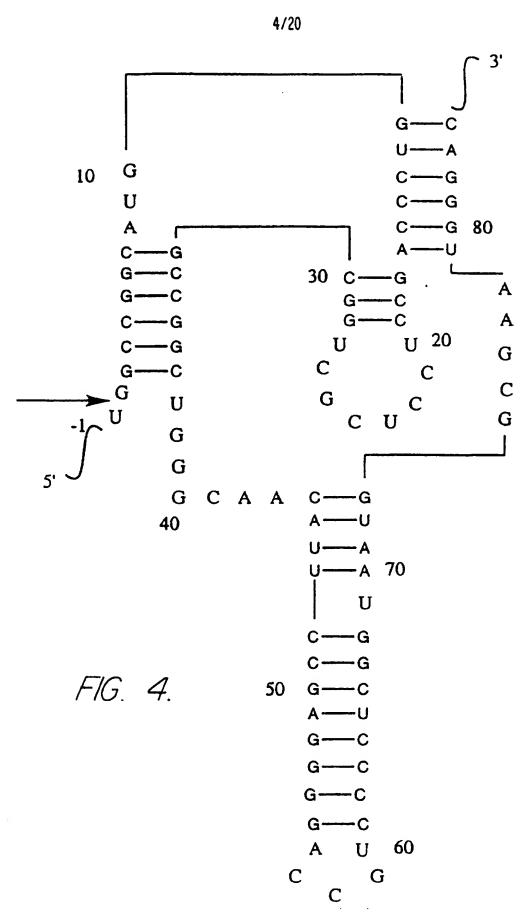
- 20. The nucleic acid molecule of claim 19, wherein, said antisense nucleic acid contain sequences complementary to the substrate nucleotide base sequences in any one of Tables II to IX.
- 21. An expression vector comprising nucleic acid encoding the antisense nucleic acid molecule of any one of claims 19 or 20, in a manner which allows expression and/or delivery of that antisense RNA molecule within a mammalian cell.
- 10 22. A mammalian cell including an expression vector of claim 21.
 - 23. The cell of claim 22, wherein said cell is a human cell.

1/20 ດັ Stem I • z • z ປຶ Cleavage Site I • Z • Z • Z z z z Z Loop II



3/20

FIG. 3.



SUBSTITUTE SHEET (RULE 26)

NEUROSPORA VS RNA ENZYME

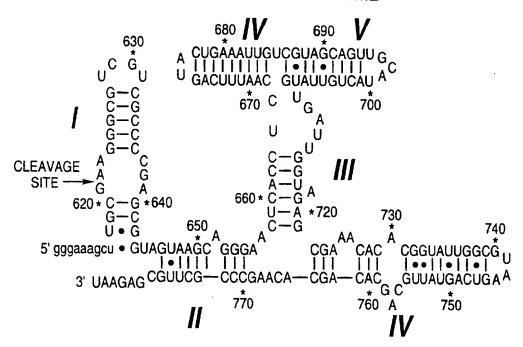
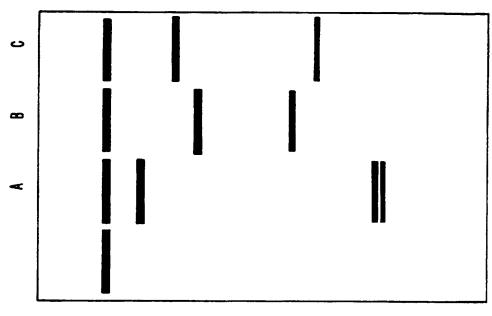


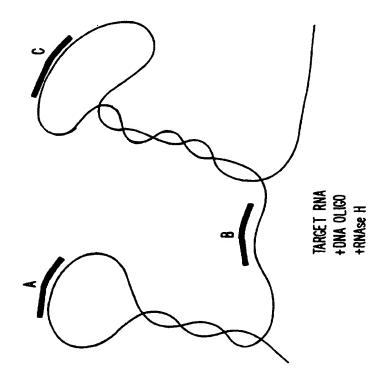
FIG. 5.

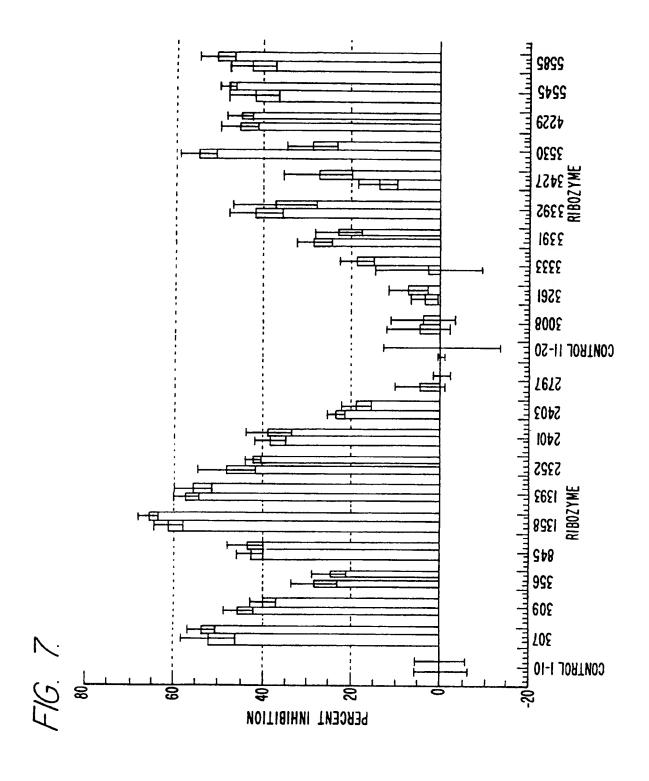
6/20

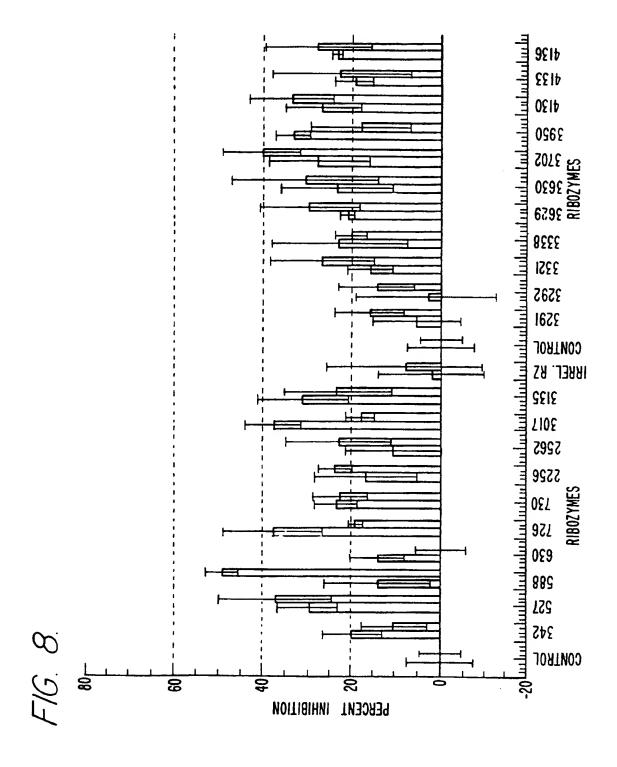


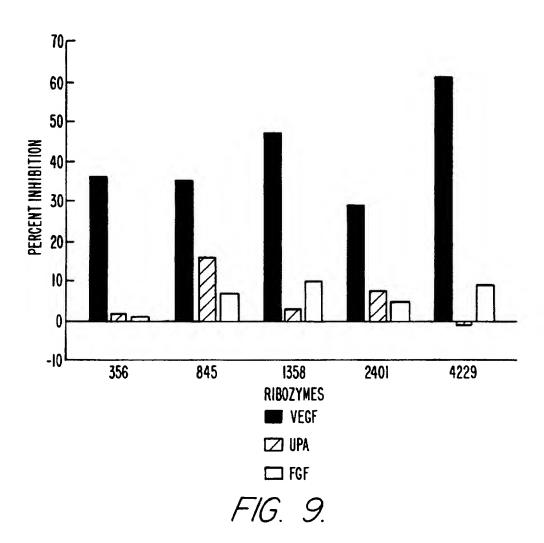
 \mathcal{O}

F16.

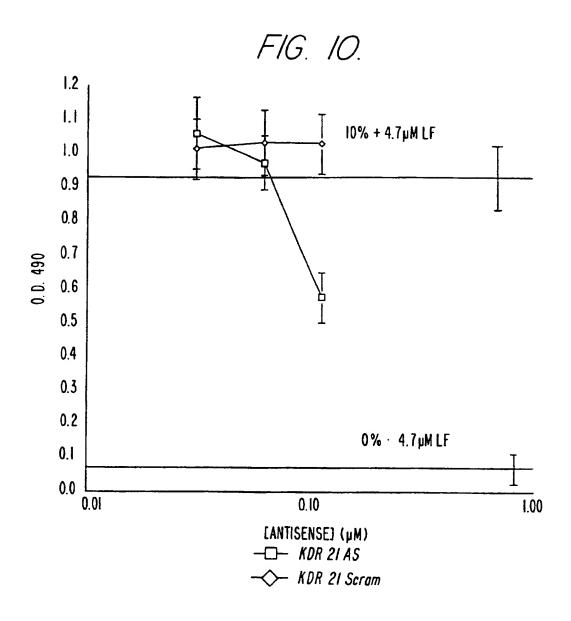


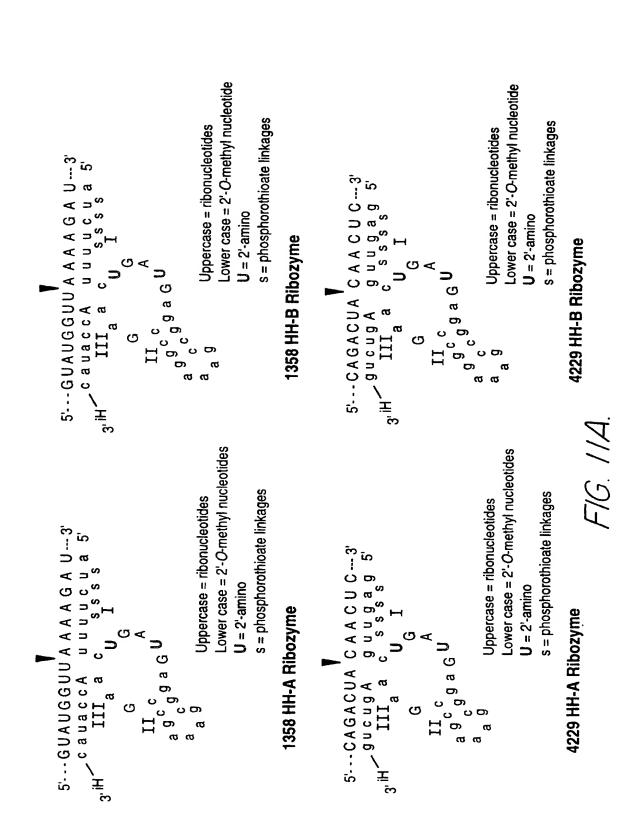






10/20





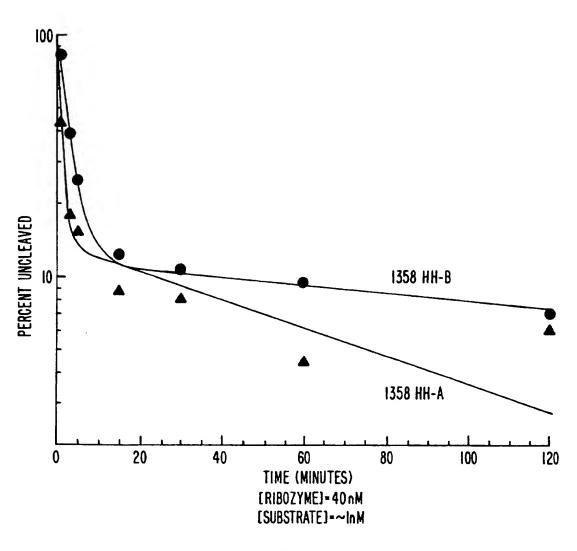
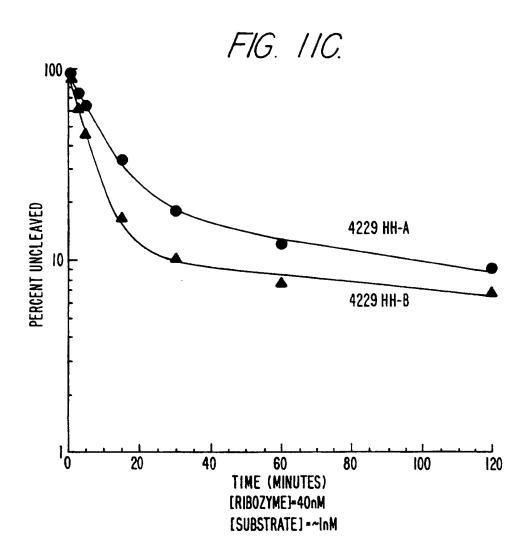
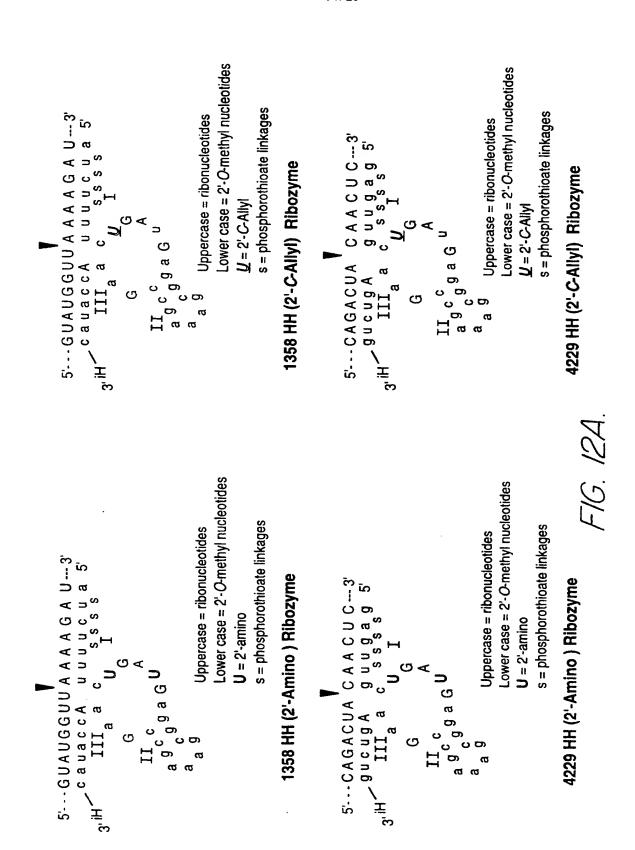
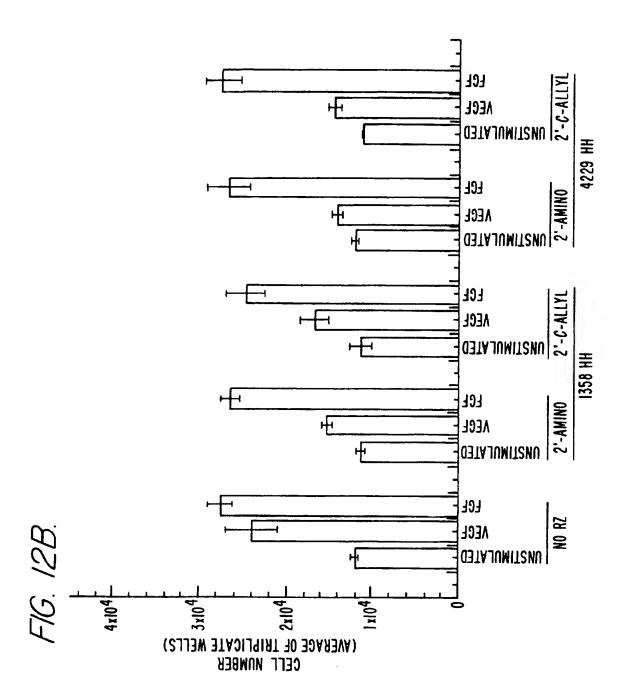


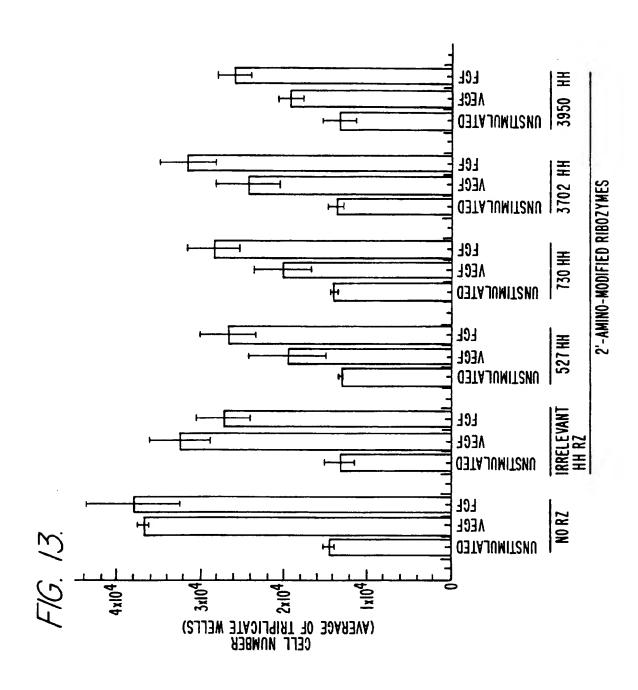
FIG. 11B.



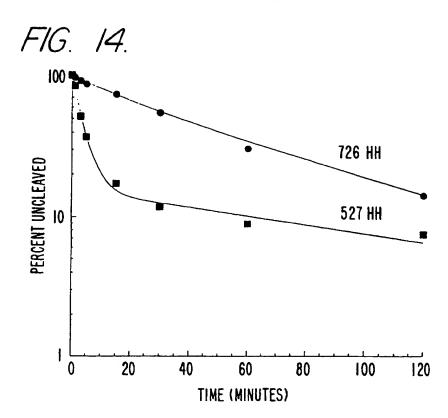
14/20

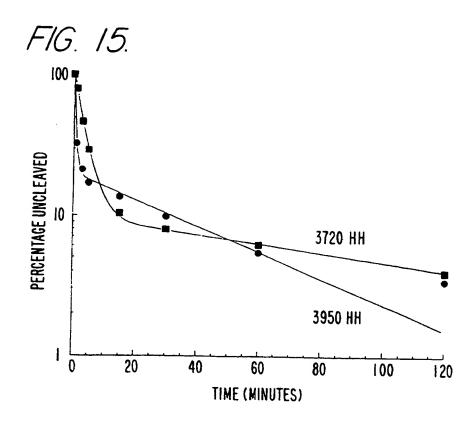




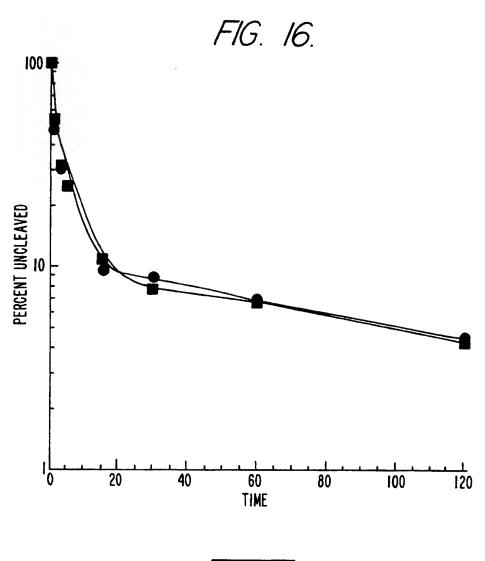


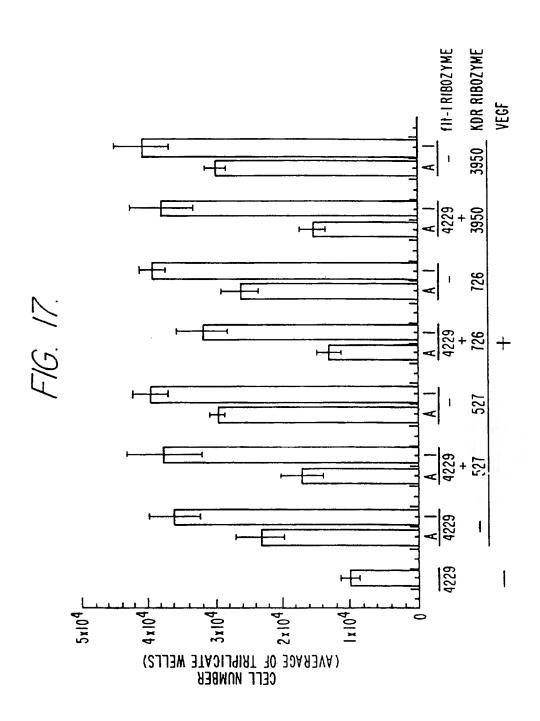




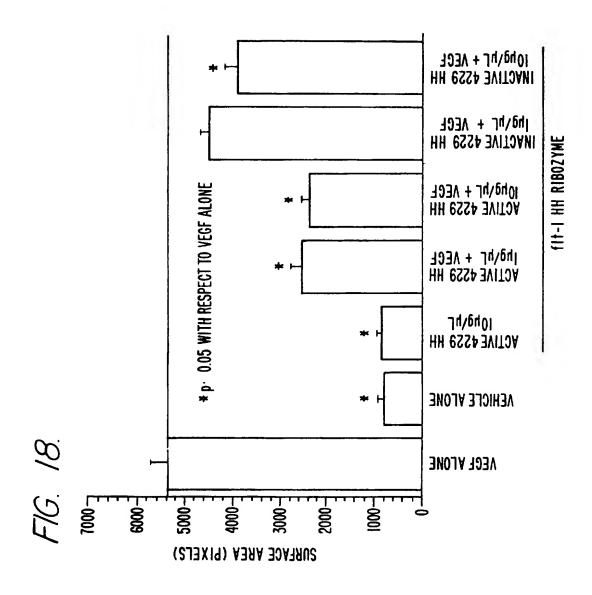


SUBSTITUTE SHEET (RULE 26)





SUBSTITUTE SHEET (RULE 26)



WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

51) Internati nul Patent Classification ⁶ : C12N 15/11, 9/00, 5/10	А3	(11) International Publication Number: WO 97/1566: (43) International Publication Date: 1 May 1997 (01.05.97)
21) Internati nal Application Number: PCT/US9 22) International Filing Date: 25 October 1996 (2)		BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC
30) Priority Data: 60/005,974 26 October 1995 (26.10.95) 08/584,040 11 January 1996 (11.01.96) 71) Applicants: RIBOZYME PHARMACEUTICAL: [US/US]; 2950 Wildemess Place, Boulder, CO 803 CHIRON CORPORATION [US/US]; 4560 Hortone Emeryville, CA 94608 (US). (72) Inventors: PAVCO, Pamela; 705 Barberry Circle, I CO 80026 (US). McSWIGGEN, James; 4866 Drive, Boulder, co 80301 (US). STINCHCOMB, Dold Post Road, Boulder, CO 80301 (US). ESC Jaime; 1470 Livorna Road, Alamo, CA 94507 (US) (74) Agents: HELLENKAMP, Amy, S. et al.; Lyon &	S, IN 301 (US on Street Frankl Dan; 720 OBED S).	(88) Date of publication of the international search report: 10 July 1997 (10.07.97) de, in 03 0.

(57) Abstract

Nucleic acid molecule which modulates the synthesis, expression and/or stability of an mRNA encoding one or more receptors of vascular endothelial growth factor.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgystan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic	SD	Sudan
CF	Central African Republic		of Korea	SE	Sweden
CG	Congo	KR	Republic of Korea	SG	Singapore
СН	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
СМ	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LR	Liberia	SZ	Swaziland
CS	Czechoslovakia	LT	Lithuania	TD	Chad
CZ	Czech Republic	LU	Luxembourg	TG	Togo
DE	Germany	LV	Latvia	TJ	Tajikistan
DK	Denmark	MC	Monaco	TT	Trinidad and Tobago
EE	Estonia	MD	Republic of Moldova	UA	Ukraine
ES	Spain	MG	Madagascar	UG	Uganda
FI	Finland	ML	Mali	US	United States of America
FR	France	MN	Mongolia	UZ	Uzbekistan
GA	Gabon	MR	Mauritania	VN	Viet Nam

INTERNATIONAL SEARCH REPORT

Interno "nai Application No PCT, US 95/17480

PC7/US 96/17480 A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/11 C12N9/00 . C12N5/10 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) C12N C07K IPC 6 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages 1-23 WO 94 11499 A (MAX-PLANCK-GESELLSCHAFT ZUR X FÖRDERUNG DER WISSENSCHAFTEN E.V.) 26 May 1994 see page 30, line 18 - page 32, line 3 1,2,19 WO 94 21791 A (J.E. BERGMANN AND X R.E.PREDDIE) 29 September 1994 see page 10, line 10 - line 26 1-23 E WO 97 00957 A (PRESIDENT AND FELLOWS OF HARVARD COLLEGE) 9 January 1997 see page 34, line 12 - line 21 1-23 WO 95 04142 A (HYBRIDON, INC.) 9 February A 1995 cited in the application see the whole document -/--Patent family members are listed in annex. Further documents are listed in the continuation of box C. X Special categories of cited documents: "I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be con-"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-"O" document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled other means document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search **30.05**.97 16 May 1997 Authorized officer Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2

5

NL - 2280 HV Rapwijk Tel. (+31-70) 340-2040, Tx. 31 651 epo ni,

Fax (- 31-70) 340-3016

Cupido, M

INTERNATIONAL SEARCH REPORT

I mational application No.

PCT/US 96/17480

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)	
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:	
1. X Claims Nos.: 16-18 because they relate to subject matter not required to be searched by this Authority, namely: Remark: Although these claims are directed to a method of treatment of the human body, the search has been carried out and was based on the alleged effect of the claimed nucleic acid molecules.	
Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:	
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).	
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)	
This International Searching Authority found multiple inventions in this international application, as follows:	
 claims 1-23 (all partly): Nucleic acid molecules specific for target sequences in the flt-1 gene. claims 1-23 (all partly): Nucleic acid molecules specific for target sequences in the flk-1/KDR gene insofar they are not included in invention 1 as defined in table X. 	
1. X As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.	
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.	
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:	
No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:	
Remark on Protest The additional search fees were accompanied by the applicant's protest. X No protest accompanied the payment of additional search fees.	

INTERNATIONAL SEARCH KERUK.

Internal Application No PC1/US 96/17480

C(Continua	non) DOCUMENTS CONSIDERED TO BE RELEVANT		Annual Ne
ategory *	Citation of document, with indication, where appropriate, of the relevant passages	R	elevant to claim No.
A	NUCLEIC ACIDS RESEARCH SYMPOSIUM SERIES, no. 31, 9 November 1994, page 163/164 XP0020020200 USMAN N ET AL: "CHEMICAL MODIFICATION OF HAMMERHEAD RIBOZYMES: ACTIVITY AND NUCLEASE RESISTANCE"		1-23

INTERNATIONAL SEARCH REPORT

.ormation on patent family members

Internal Application No
PC1, US 96/17489

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9411499 A	26-05-94	AU 5562794 A CA 2149298 A CN 1094445 A EP 0669978 A JP 8505763 T	08-06-94 26-05-94 02-11-94 06-09-95 25-06-96
WO 9421791 A	29-09-94	NONE	
WO 9700957 A	09-01-97	AU 6288496 A	22-01-97
WO 9504142 A	09-02-95	AU 7516894 A CA 2167680 A CN 1131437 A EP 0711343 A FI 960374 A NO 960303 A	28-02-95 09-02-95 18-09-96 15-05-96 25-03-96 13-03-96